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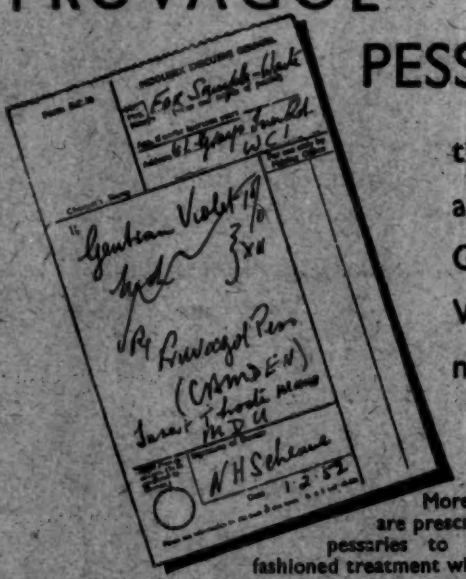

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BRITISH MEDICAL JOURNAL

LONDON SATURDAY APRIL 19 1952

THE FIFTH AND SEVENTH CRANIAL NERVES IN RELATION TO THE NERVOUS MECHANISM OF TASTE SENSATION*

A NEW APPROACH

BY

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Since the days of Magendie and Claude Bernard, over a hundred years ago, many and varied opinions have been held or suggested concerning the nerves supplying the sense of taste to the front and back of the tongue. Magendie, in 1822, declared that after intracranial section of the trigeminal nerve in dogs taste is completely lost, even for sour and bitter. Bernard, in 1831, following Bellingeri in 1818, showed that the chorda tympani running with the facial nerve conducted taste from the tongue. Yet apparently he agreed with Magendie's statement regarding the gustatory function of the fifth nerve, for he never denied it or referred to it in his writings. Lussana, in 1869, described two cases : one of destruction of the fifth nerve, with complete anaesthesia of one side of the face and tongue, in which no impairment of taste was found ; in the other case the facial nerve had been divided accidentally by a charlatan, resulting in complete loss of taste on the anterior part of half the tongue, which Lussana found on examining the man two years later. Many cases have since been published of loss of taste on the tongue associated with gross disease involving the fifth nerve at the base of the skull.

Whether the fifth nerve or the chorda tympani was the conducting nerve of taste sensations, the ultimate peripheral receptors of gustatory sensation have for many years been associated with taste buds mainly on the front and back of the tongue, those on the back of the tongue being innervated by the glossopharyngeal nerve, and those on the front, especially the sides and the tip, by the chorda tympani, the dorsum being relatively insensitive to taste. The four modalities of taste perception—sweet, bitter, salt, and sour—have been recognized by physiologists as distinct, and mainly represented in certain areas of the tongue, sweet and salt especially near the tip, sour laterally, and bitter especially at the back. More recently these four modalities are believed to depend on different receptors, probably arranged zonally (Patton and Ruch, 1949), and supplied by chorda tympani or glossopharyngeal fibres respectively. In favour of this view is the known effect of certain drugs applied to the tongue in temporarily abolishing one or other of the four primary taste sensations. Thus, the chewing of leaves of *Gymnema sylvestre* abolishes taste for sweet and bitter, and phenylthiocarbamide, which tastes bitter to most people, is tasteless in about 20% of those tested. According to Wiggers (1949) taste blindness, in which one or more of the primary sensations may be weak or absent, is not uncommon, and is hereditary as a Mendelian recessive. Sodium benzoate, a common food preservative, is tasteless for the majority, but may be called sweet or bitter by 25% of persons tested.

The 130-year-old controversy whether the fifth nerve or the chorda tympani is the central conducting path for taste from the tongue has now for many years been considered settled in favour of the chorda tympani. The object of this paper is to bring fresh proof of the importance of the fifth nerve in taste perception, not as the central continuing path from the tongue, but as furnishing in the large majority of people a necessary blending of fifth-nerve sensibility with the primary gustatory function of the chorda tympani and its receptors. The Diagram overleaf shows the course of the taste fibres and of the intrapontine connexions of the fifth nerve. In a small minority of persons the fifth-nerve sensibility is of very slight and temporary importance ; in a large number its importance is great, taste being lost for weeks, months, or years after fifth-nerve lesions ; and in a small minority, at the other end of the scale, this loss appears to be permanent.

Further, I wish to draw attention to the gustatory function of the great superficial petrosal (Vidian) nerve in supplying the palate, comparable to that of the chorda tympani on the tongue, in less degree, and to point out that palatal loss of taste usually occurs in lesions of the maxillary nerve or of the Gasserian ganglion which cause palatal anaesthesia to touch and prick, and, moreover, that geniculate ganglion or pars intermedia lesions, with or without accompanying facial palsy, produce palatal loss of taste in these cases without palatal anaesthesia.

Many writers have produced statistics intended to prove that taste is not lost in fifth-nerve lesions. Lewis and Dandy (1930), as the result of tests after fifth-nerve-root section for trigeminal tic, concluded that the chorda tympani is the only conducting path for taste sensations on the front of the tongue, and that the fifth nerve has no connexion with taste. Schwartz and Weddell (1938),

*A Clinical Lecture delivered at St. Mary's Hospital, November 30, 1951.

dealing with similar root-section operations at St. Louis, mostly by Sachs, quote four cases with no taste loss examined a few days after operation, and others in which loss of taste was stated to be due to damage to the Vidian nerve, with or without facial palsy. They quote loss of taste found on the tongue five days after root section, with deliberate section of the Vidian nerve but without facial palsy, as evidence of conduction of taste by the Vidian nerve from the tongue, and not by the chorda tympani. They completely ignore the tactile and pain analgesia of the tongue as a factor in the loss of taste, and conclude that in certain individuals the Vidian nerve forms part of the pathway for taste from the front of the tongue, though they cannot explain how these taste sensations reach the Vidian nerve. Carmichael and Woollard (1933) examined 17 cases of total fifth-nerve anaesthesia after Gasserian alcohol injection. They found that 10 cases of the 17 had complete ageusia on the anterior anaesthetic half of the tongue, but were unable to give any explanation of the variations found.

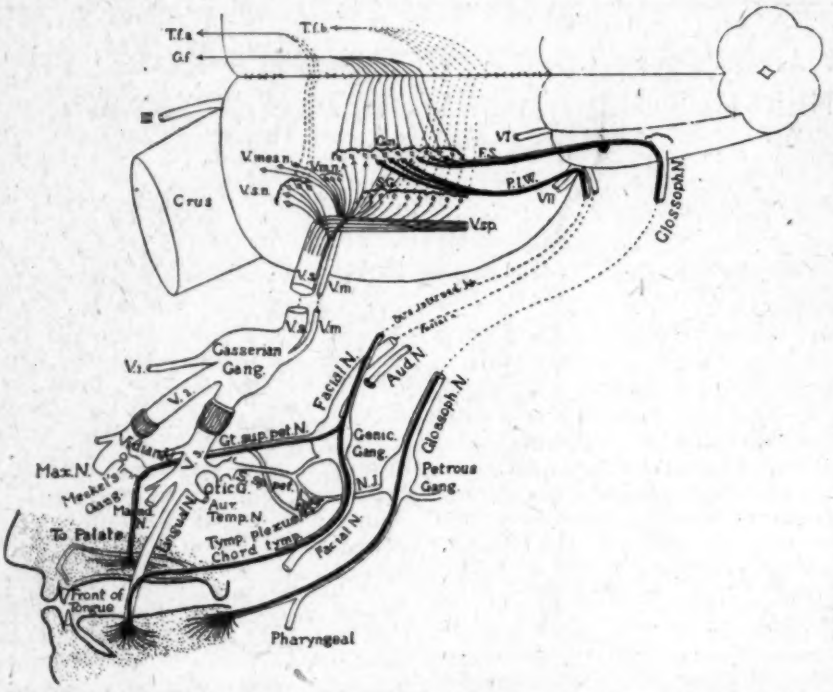

Diagram of the course of the taste fibres (thick lines) and of the intrapontine connexions of the fifth nerve. (The lower half is represented in profile, and the upper in plan. For convenience the gustatory nucleus and substantia gelatinosa are represented in the pons instead of in the medulla.)

T.f.a.: Trigeminal fillet (tactile and pressure).
T.f.b.: Trigeminal fillet (pain and temperature).
G.f.: Gustatory fillet.
III: Third cranial nerve.
VI: Sixth nerve.
V.mes.n.: Fifth mesencephalic nucleus.
V.m.n.: Fifth motor nucleus.
G.n.: Gustatory nucleus.
F.S.: Fasciculus solitarius.
V.s.n.: Fifth sensory nucleus (tactile and pressure).
S.G.: Substantia gelatinosa (nucleus of fifth spinal root).
VII: Roots of the seventh cranial nerve (facial).
V.sp.: Fifth nerve, spinal root.
V.s.: Fifth nerve, main sensory root.
V.m.: Fifth nerve, motor root.
V.1.: Ophthalmic branch, fifth nerve.
V.2.: Maxillary nerve.
V.3.: Mandibular nerve.
N.J.: Nerve of Jacobson.
P.I.W.: Pars intermedia wrisbergi.

The chorda tympani and great superficial petrosal (Vidian) nerves carrying taste impressions from the front of the tongue and palate respectively are shown uniting in the pars intermedia wrisbergi. (See Harris, 1926, p. 252.) The glossopharyngeal carries taste impressions from the back of the tongue to the fasciculus solitarius.

The Views of Gowers

Gowers held the strong belief that taste sensation was ultimately conveyed to the pons by the fifth nerve, though he agreed that the peripheral pathway was via the fibres of the chorda tympani, lingual, and facial nerves to the geniculate ganglion. He stated definitely that no taste fibres accompanied the facial nerve within the skull, but that they must leave the geniculate ganglion by the great superficial petrosal (Vidian), passing to Meckel's ganglion and thence by the second division of the fifth nerve to the Gasserian ganglion and pons. Gowers was a most careful clinical observer, and, although his statements of loss of taste in numerous cases of fifth-nerve lesions date back 60 years or more, that is no reason to disbelieve them *in toto*. He writes in 1893 (p. 226): "In almost every case I have seen in which there were symptoms of disease of the root of the fifth nerve I have found taste abolished on the corresponding side, not only on the front of the tongue but also on the back of the tongue, and on the arches of the palate. On the other hand, cases occur in which there are symptoms of disease of the fifth nerve without loss of taste." These variations, to my knowledge, he did not attempt to explain.

When I was Gowers's house-physician at the National Hospital in 1896 I had the opportunity to examine a man he sent into the hospital for one of his Wednesday lectures, a groom, aged 46, who ten months previously had suffered with pain for six weeks in all his teeth on the left side, followed by numbness of the left side of the face and mouth. He had right-sided cerebral facial weakness, complete left fifth-nerve anaesthesia and motor palsy, with total loss of taste on the anterior portion of the tongue on the left side, and left frontal herpes. The lesion was no doubt a gumma on the roots of the left fifth nerve, pressing on the side of the pons. He soon recovered completely after a course of mercury and iodide of potassium. This case I published, with photograph (Harris, 1926, p. 243). I have also full notes of another case of Dr. Gowers's.

Mrs. Clara O'Leary, aged 50, was admitted to the National Hospital on August 13, 1896. This is obviously the case that Gowers referred to in a footnote to page 226 of his textbook, which he had seen on July 5, 1880, and which he published in the following year (Gowers, 1881). She was then 33, and woke up during the night of April 14 with a burning sensation in the right side of the face, and found at once she had no feeling there. On the 17th her doctor found complete loss of sensation in all parts supplied by the right fifth nerve. Nearly three months later Gowers observed that the muscles of mastication were very weak and wasted, and that taste was absolutely lost to salt, sugar, and quinine on the right half of the tongue, front and back, and on the anterior palatine arch, and in the region of the tonsil, where common sensibility was normal. This absence

of taste on front and back of tongue Gowers (1897) states was still unaltered seven years later. Taste was acute on the left corresponding areas. There was some diplopia due to the third and sixth nerves. His comment on the case was that this patient had but one nerve of taste, the fifth.

When I examined her, 16 years later, she stated that she had never recovered any sensation on the face, and I found that she still had complete anaesthesia to touch and prick over the whole area of the right fifth nerve to the midline, including the hard palate, and complete atrophy of all the muscles of mastication on the right side. Taste was also completely lost on the front two-thirds of the tongue on the right side, but she could recognize sweet, salt, and bitter on the right back of the tongue, though much less than on the left side. Taste had evidently partly returned on the right back of the tongue in the intervening 16 years, which corresponds entirely with the partial recovery of taste I have often observed on the front half of the tongue after Gasserian ganglion injections. She had also developed right sixth-nerve palsy, which is shown in the photograph here reproduced.

The explanation of the partial return of taste on the back of the tongue, while taste was still completely absent on the front portion, would appear to be that this area was shared between the glossopharyngeal and fifth-nerve common sensibility, and not, as Gowers thought at first, that the glossopharyngeal had no taste supply in her case. Nearly a year afterwards, in May, 1897, her right facial nerve became completely paralysed. Whatever the pathological diagnosis may be here, the special interest of the case is the total loss of taste on the right front and back of the tongue, associated with total fifth-nerve paralysis, vouched for 16 years before by Gowers, and again reported on after careful revision in 1896.

Loss of Taste in Various Fifth-nerve Lesions

Loss of taste on the front half of the tongue I have also seen in two of Victor Horsley's gasserectomies, and in one operated on in 1929 by Mr. Cairns, in which I found complete loss of taste on the front half of the tongue 14 days after the operation. In a woman, aged 57, under my care in October, 1942, for acoustic neuroma, which was successfully operated on a month later, numbness of the right side of the face, with pain, had been present for ten months, with total trigeminal anaesthesia and complete loss of taste on that side of the front of the tongue. Cushing found temporary loss of taste on the anaesthetic half of the tongue in a few of his Gasserian cases, but discounted its importance by explaining it as due to descending degeneration of the lingual nerve causing pressure on the chorda fibres which run with it. This explanation must be fallacious, for I have dozens of times demonstrated total loss of taste on half of the tongue immediately after alcohol injection of the third division of the fifth nerve, or after Gasserian injections, usually done under a local analgesic only.

In 1926 I published notes of 26 cases of complete loss of taste on the front half of the tongue, out of 80 observed cases of such loss after alcohol injection (Harris, 1926, p. 265), and in 1940 I referred to 167 cases of loss of taste I had found after similar injections. This number has now increased to well over 200, and among these are several in which I have observed that the loss still existed many months and even years after injection.

A woman aged 40, whom I saw first in 1908 for neuralgia of six years' duration of the left second division, had an injection of the second division in front of the foramen rotundum in February, 1909; this gave complete relief, with dense anaesthesia for three years. In 1915 I injected her left Gasserian ganglion, producing total left trigeminal anaesthesia, with complete loss of taste on the left front half of the tongue. This condition persisted unchanged for 24 years; when I saw her in 1939 I found that the anaesthesia and the loss of taste were still complete as before, though taste was acute on the right side.

A man aged 33, whom I saw first in November, 1914, for severe neuralgia of the right second and third divisions for the past three years, had a Gasserian injection which produced dense right trigeminal anaesthesia, with loss of all taste on the right front half of the tongue. Pain recurred after five years' relief, and reinjection was followed by a further eight years' relief. In 1929 I again injected the ganglion, this time with permanent success. I saw him on May 2, 1951, and found the trigeminal anaesthesia still complete, and the loss of taste as before, 22 years after the last injection.

Other records I have, of four cases showing loss of taste still existing, with anaesthesia of the front half of the tongue, 7, 11, 13, and 15 years after Gasserian injection, and of numerous other cases in which it was present for periods up to two and three years. I have also seen taste return to the front half of the tongue five years after Gasserian injection, though it was still absent after two years.

Bilateral trigeminal tic I have met with in 108 cases, roughly 4–5% of all cases. Usually a considerable interval occurs before the second side is affected—in one case 67 years, the initial attack on the right side occurring at the age of 12 and that on the left side at 79. On more than one occasion less than a week had elapsed before the attacks became bilateral, the severity being about equal in intensity. In others, one side, usually but not invariably the second to be involved, may not be affected severely enough to require injection or operation. Bilateral ganglion injection may be necessary, and I have several times seen total loss of taste on both sides of the front of the tongue, while taste remained acute over the glossopharyngeal area.

Loss of Taste on Back of Tongue, with Fifth-nerve Anaesthesia

Complete hemi-ageusia on the front and back of the tongue must, I think, be rarer than Gowers has suggested in fifth-nerve lesions. I have found this total loss in a few of my Gasserian injections, and have notes of eight such cases. One recent case illustrates this point well.

An intelligent woman secretary aged 43 was injected for trigeminal tic, though the history did not accord entirely with the classical type, as eating and talking did not start the paroxysms, nor had she trigger zones. Relief was only temporary for two weeks, though the anaesthesia seemed complete at first, and I repeated the injection on February 20, 1950, after which the anaesthesia remained apparently complete and taste was entirely lost on both the front and back of the tongue, palate, and pharynx on the left side. Not only was taste lost, but there was also complete anaesthesia over the left side of the pharynx and tonsillar region, as exploration with a hatpin proved conclusively. Gowers (1893, p. 216) also states: "It is certain that disease of the fifth nerve may cause anaesthesia in the root of the tongue and palate."

As the neuralgia again returned within two to three weeks of the second injection, I became suspicious of basal tumour pressing on the root of the fifth nerve, and I persuaded Sir Hugh Cairns and Mr. Pennybacker to investigate her at Oxford, which was done most carefully by encephalogram, C.S.F. examination, and vertebral angiogram, so that they felt confident there could be no basal or other cerebral tumour, which I had begun to suspect. They agreed that the trigeminal anaesthesia was complete, but as a last resort Mr. Pennybacker resected the left fifth sensory root in January, 1951, with complete success. I saw her and examined her again in July, when she told me that as soon as she began to come round from the anaesthetic she knew that her pain had disappeared, and there has been no recur-

rence since. The anaesthesia seemed on testing to be the same, and the taste loss on the front and back of the tongue and on the soft palate and pharynx on the left side still remained complete, six months after the operation. Some few nerve cells and fibres must have escaped alcohol destruction, though undetected on most careful sensory testing before the operation.

What is certain is that in a few cases of trigeminal anaesthesia loss of taste includes the back of the tongue as well as the front half, and when this is the case the loss of taste is more likely to be of long duration. I am convinced from my experience that taste is lost at first in nearly every case when anaesthesia of the front half of the tongue is complete, but that it is regained at varying intervals, maybe of hours only, or days, weeks, months, or years. An explanation of this fact is discussed below.

Palatal Anaesthesia, with Loss of Taste

In all the records of testing for taste that I have read, the palate is scarcely, if ever, mentioned. It is true that taste buds are much more sparsely found in the palate than on the front or back of the tongue, yet taste may be quite acute on the soft palate in many people. When testing, however, considerable care is required to avoid touching the tongue with the testing material. A broad electrically illuminated spatula should be used to keep the tongue down while a camel-hair brush soaked in syrup, salt solution, quassia, or quinine is used to paint the solution on the front half of the soft palate. The patient is not allowed to speak, but must be instructed beforehand to point to one of four cards on which are clearly written "sweet," "salt," "sour," "bitter." If no taste is perceived after the lapse of ten seconds, then the test is repeated on the other side. It may be that neither side is responsive enough to make the test valid; in that event, after the mouth has been washed out with warm water, the tests are repeated with a different substance. Some people are quite unable to distinguish different tastes on the palate, but may definitely taste something on the normal side when no sign of any taste may be perceived on the anaesthetic side. In others the perception and differentiation of taste may be quite acute and immediate on the normal side when it is completely absent or uncertain on the anaesthetic side.

When the second trigeminal division is involved with the third in a Gasserian injection taste is usually lost in the early days on both tongue and palate. Such palatal loss of taste cannot be concerned with the chorda tympani, but must be due either to second division anaesthesia or to loss of gustatory conduction by the great superficial petrosal nerve. I have injected the inner half only of the Gasserian ganglion in numerous cases of migrainous and ciliary neuralgias, and in some cases of trigeminal tic, when the pain is limited to the first or second division, or both. This is not particularly difficult to do, and complete escape of the third division from anaesthesia is a great advantage to the patient in eating and drinking; the absence of loss of taste on the tongue is also of benefit. I have seen similar loss of taste with palatal anaesthesia in cases in which I have injected the second division alone in front of the foramen rotundum, also in a case of temporo-sphenoidal gumma with complete anaesthesia of the upper jaw, cheek, and palate, as well as in a case of acute herpes zoster of the second trigeminal division only, with total anaesthesia of upper jaw and cheek. In these cases there can be no lesion of the great superficial petrosal nerve—which is, in my belief, the afferent gustatory nerve from the palate, via Meckel's ganglion to the geniculate ganglion and pars intermedia—for the lesion in the maxillary nerve is well away from this area.

Palatal Loss of Taste in Facial Paralysis

I will now return to facial paralysis, and the common accompanying loss of taste on the tongue, in those cases of facial damage between the geniculate ganglion and the exit of the chorda tympani in the middle ear to join the lingual. Peripheral lesions of the facial nerve at or below the stylo-mastoid foramen are not accompanied by any loss of taste, unless inflammation spreads upwards along the nerve to include the chorda fibres in the aqueduct of Fallopius. On testing the palate in many cases of facial paralysis I have found that loss of taste is present on the palate as well as on the tongue. In these cases, also, the chorda tympani is not directly concerned with the palatal loss; but this is easily explained if the lesion causing the facial palsy is at or above the geniculate ganglion, where the chorda is joined by the great superficial petrosal to form the pars intermedia Wrisbergi. The lesion thus interrupts not only the chorda but the great superficial petrosal, which is almost certainly the supplier of taste fibres to the palate.

The course of the stimuli is therefore via the main palatal nerve, Meckel's ganglion, and Vidian nerve (great superficial petrosal) to the geniculate ganglion, and not in the reverse direction, as Gowers believed. A. F. Dixon (1897) wrote: "The great superficial petrosal is formed very early, and is developed as an outgrowth of the cells in the geniculate ganglion, proving that it conducts towards the geniculate ganglion. The same argument applies also to the chorda tympani, and to the nerve of Jacobson, which is an outgrowth of the petrous ganglion on the glossopharyngeal nerve, and therefore conducts towards the glossopharyngeal, and not to the trigeminus, as Gowers suggested."

Indeed, the presence or absence of loss of taste on the palate may be regarded as a clue to the position of the lesion in cases of facial paralysis. Any lesion causing facial palsy, at or above the geniculate ganglion, before the pars intermedia leaves the facial motor nerve to enter the medulla, should cause loss of taste on the palate as well as on the tongue. Gowers (1893, p. 227) stated: "Disease of the facial nerve within the skull does not impair taste"; but this is disproved by modern evidence. Dandy (Lewis and Dandy, 1930) found loss of taste on the tongue in cases in which he divided the facial within the skull, and I have seen taste loss produced on both the tongue and the palate in two cases, without any anaesthesia of the tongue, when I injected the inner half of the Gasserian ganglion. Some leakage of alcohol took place into the cave of Meckel, and must have spread backwards to the internal auditory meatus, setting up the vestibular syndrome, severe vertigo, coarse nystagmus to the opposite side, nausea and vomiting, faintness and pallor, and, if more than two or three drops of alcohol have leaked, nerve deafness and facial palsy. The facial palsy is likely to last for several weeks, but in my experience it has resolved. Permanent deafness I have seen occur only once, when a surgeon injected 2 ml. of alcohol into the Gasserian ganglion under a general anaesthetic.

Some Statistics Concerning Trigeminal Tic

I have notes of 2,083 cases of trigeminal tic, and have seen a great many more in various hospitals, especially St. Mary's, of which I have kept no notes. Of these 2,083 cases, 1,382 were women and 701 men, nearly a 2 to 1 ratio. Of this total 68 also suffered from chronic spastic paraplegia, of which the large majority were undoubtedly cases of disseminated sclerosis. One case was certainly a syphilitic paraplegia, and one other possibly amyotrophic lateral sclerosis, though the disease was very chronic. Therefore 3.1% of all the 2,083 cases of tic were complicated by disseminated sclerosis. I have also seen trigeminal tic complicating other diseases: three cases of tabes, two being bilateral tic, one each of Friedreich's disease, peroneal atrophy, Parkinson's disease, achondroplasia, and acromegaly. The average age of onset of tic in these 2,083 cases was 51.87 years—being 51.34 for women and 52.93 for men. Glossopharyngeal tic is very much rarer in my experience, with 20 cases (11 female and 9 male), one case being bilateral and one also suffering from trigeminal tic. The comparative frequency is probably in the neighbourhood of 1 to 200. I have never met with a case of disseminated sclerosis complicated by glossopharyngeal neuralgia, but Dr. Purdon Martin tells me he has seen one such case.

It is not very uncommon in the early stages of disseminated sclerosis for temporary numbness of one side of the face, with trigeminal anaesthesia, to develop rapidly without any pain then or subsequently. The numbness usually passes off in about two months. I have seen four such cases, of which I have notes that there was complete loss of taste accompanying the anaesthesia of the front half of the tongue, which the patient was aware of before being tested.

As to the age of onset in trigeminal tic, three-fifths of all the cases begin between 40 and 60. It is comparatively rare for the disease to begin after 80, but I have seen bilateral tic in a woman of 90, in whom I had to inject both Gasserian ganglia on succeeding days. This of course produced temporary jaw-drop and some difficulty in feeding for about three months, much to the indignation of the patient and her daughter; but the motor palsy always resolves, owing to the motor nucleus lying in the pons, out of harm's way. The daughter wrote to me when her mother was 93, saying that she was in good health and taking her food fairly well.

Many cases of trigeminal tic begin in the twenties, but only a few in the second decade. I reported the remarkable case of a small girl in whom trigeminal tic of the left third division certainly started as early as 16 months (Harris, 1943). The pain was at first naturally ascribed to teething, though the sudden short attacks of screaming were typical of tic. Her teething was late, beginning at 12 months, and was not complete until she was 3 years old. From that age there could be no doubt, from the mother's account, that the pain was limited to the left side, especially the lower jaw. I did not see the child until she was 4 years and 5 months old, when she was brought to me in the outpatient department of Maida Vale Hospital, on July 3, 1942. There could be no question about the diagnosis; I witnessed several attacks, in which she would moan and grizzle, with her hand to her left cheek for a few seconds, and then be immediately merry and bright until the next attack. *X*-ray films, reported on by Harrison Orton, of St. Mary's Hospital, showed that the teeth and mandible were normal for her age. Medicines had no effect, many spasms recurring daily, so on August 21 I tried to inject V.3 under general anaesthesia. It was not until my fifth attempt, on December 9, that I succeeded in injecting the left Gasserian ganglion with 0.5 ml. of alcohol. This produced total trigeminal anaesthesia, and with the exception of transient slight keratitis, which quickly yielded to treatment, she has had no recurrence of neuralgia. She takes no special precautions, and when last seen two years ago was quite well.

The Path of the Taste Fibres to their Cerebral Terminations

There can be little if any doubt now that the gustatory fibres of the chorda tympani and the great superficial petrosal (Vidian) nerves pass centrally to the geniculate ganglion, and thence by the pars intermedia to the medulla and pons. Their course and central terminations were carefully worked out 45 years ago by Nageotte (1906), physician and pathologist to the Bicêtre Hospital in Paris. He followed the Marchi degeneration of the fibres of the pars intermedia in the medulla. A patient had died from secondary carcinoma, with a recent unilateral facial palsy, and a small seed-like secondary growth was found in the chorda tympani just below the geniculate ganglion. No Marchi degeneration, of course, was found in the pars intermedia on the central side of the ganglion until the fibres pierced the side of the medulla, after shedding their sheaths of Schwann. He traced them into a nucleus continuous below with the substantia gelatinosa surrounding the fasciculus solitarius, or descending branch of the glossopharyngeal nerve. This nucleus reaches as high as 2 mm. below the convolutio trigemini, and is 14 mm. in length. He names it the gustatory nucleus, the pars fibres occupying the median 8 mm. and joining with the glossopharyngeal fibres below, and above with numerous trigeminal fibres which he traced into the upper portion of the nucleus. From this nucleus doubtless secondary fibres decussate to run upwards on the other side of the medulla and pons, close to the middle line, which may be called the gustatory fillet, which runs separately on the inner side of the median sensory fillet and its trigeminal portion. Evidence of its almost median situation is afforded by clinical cases of pontine thrombosis and pontine glioma, and by a published case (Harris and Newcombe, 1926) of syringobulbia with unilateral lesions of cranial nerve nuclei, but with bilateral ageusia. Nageotte thought the fifth-nerve fibres which he described as entering the rostral portion of the gustatory nucleus were true taste fibres, but this view should now be discarded.

Before accepting the view that the fifth nerve contains true gustatory fibres it must be demonstrated that taste persists or returns on the tongue after destruction of the chorda tympani, which would be comparable to the frequent preservation or return of taste after total destruction of the fifth nerve.

The thalamic termination of the gustatory path is believed to be the postero-ventral nucleus, whence taste sensations were formerly stated to be relayed to the hippocampal gyrus, near the olfactory centre, partly because of the frequent association of taste and smell in recognizing and distinguishing certain flavours. Börnstein (1940) pointed out that taste appears to be even more closely related to somatic sensation of the mouth and tongue than to olfaction, a view which harmonizes completely with my assumption of a welding of fifth-nerve tactile and pain sensibility with the gustatory sensations initiated by the chorda tympani in the front of the tongue and by the Vidian in the palate, the glossopharyngeal common sensibility with its gustatory fibres supplying the back of the tongue. Penfield and Erickson (1941) locate the cortical centre in the inferior portion of the post-central area, which Börnstein (1941) defines as the foot of the post-central gyrus in the parietal lobe just behind the motor chewing centre in the precentral gyrus.

The Share of the Fifth Nerve in Taste Perception

The apparent conflict of views on the gustatory function of the chorda tympani and great superficial petrosal (Vidian) nerves on the one hand, and of the fifth nerve on the other, is to be explained by assuming that there is a correlation or welding of the sensibility of the tongue and palate supplied by the fifth nerve with the true gustatory sensations from the chorda and petrosal nerves. In normal people taste is therefore perceived through the dual function of normal sensibility of the fifth nerve and the gustatory stimuli supplied by the chorda and Vidian nerves. In all cases of total lesion of the chorda and Vidian nerves, as may occur in geniculate herpes, or in facial palsy due to a lesion at or above the geniculate ganglion, taste will be permanently lost on the front half of the tongue and palate, the normal sensibility of the fifth-nerve supply to those parts being quite unable alone to provide a taste sensation.

In the great majority of persons a complete lesion of the mandibular and of the maxillary nerves will abolish the tactile, pain, and thermal perceptions on the tongue and palate, and the chorda or petrosal nerve alone may be insufficient at first to arouse the sensation of taste. In some persons this welding of the tactile and pain stimuli on to the gustatory function of the chorda and Vidian nerves is so important that taste is never regained, as is shown in many of my records, as well as in numbers of cases published by Gowers and others of permanent loss of taste in fifth-nerve lesions. In most people taste is gradually regained after fifth-nerve lesions, after varying intervals of hours or days to weeks, months, or even years, according to the extent of dependence on the tactile, pain, and thermal stimuli of the fifth nerve in the combined gustatory sensation of the individual. In a small minority —I have met with between 30 and 40 such cases—no loss of taste is found a week or two after total anaesthesia to

touch and prick has been produced by interruption of the third division of the fifth nerve, or by complete Gasserian destruction, or by sensory root resection.

As I have shown, a total second division lesion or an inner ganglion injection produces loss of taste on the palate without any anaesthesia or loss of taste on the tongue. I have no record of return of taste on the palate in such cases, but I have no doubt that it would occur in many of the cases, just as taste returns in the majority of third division or Gasserian cases.

Reaction Time

This varying dependence in different individuals on the share in taste perception of the normal sensibility of the tongue and palate is shown by the fact that many normal persons, when tested with the tongue kept protruded, are unable to name the variety of taste, whether sweet, salt, sour, or bitter; when, however, the tongue is withdrawn and moved around in the mouth, the correct answer is given after a few seconds. Others, again, are quick in indicating their recognition of the variety of taste within one or two seconds of the testing solution being painted on the side of the front of the tongue. Others are so slow in recognizing varieties of taste that they may make mistakes even after withdrawing the tongue within the mouth. This variation in speed and accuracy of reply is even more marked when testing the half-palate. I have, however, in many cases been able to obtain definite results in testing the palate, especially in persons of quick intelligence, though much less so in old people of poor education. It has been stated that two-thirds of the taste buds may be atrophied in old age.

The speed of reaction times in the full recognition of taste may advantageously be compared with the reaction time to a touch or prick on the tongue, or of the three other special senses of sight, hearing, and smell. A flash of light, the sound of a bell struck near by, or a pin-prick on the tongue is practically instantaneously recognized; even a sense of smell, whether pleasant or unpleasant, is almost as rapidly recognized, though inhalation is necessary and the varieties of scent will take longer to differentiate.

If we take four small bottles containing water, salt, sugar, and bitter solutions at the same room temperature, and with a medium-sized camel-hair brush sweep a brushful of water across the front of the tongue of a normal adult assistant, nothing except the touch is noticed. But when, after drying the protruded tongue with a clean handkerchief or white blotting-paper, a similar brushful of one of the three other solutions is used, an immediate marked difference in sensation is felt, often as a chilly or slightly smarting sensation, but not as a definite taste at first, though "sweet," "salt," or "bitter" may be pointed to—often wrongly—and it is not as a rule for several seconds that the correct taste is fully appreciated. The time of reaction varies much in different persons, probably owing to the different degree in which the individual is dependent on fifth-nerve sensibilities; yet the reaction time is far longer than that to pin-prick on the tongue, or to a flash of light, or to a sudden clang of a bell. This delayed reaction to taste may be understood when we consider the different method of appreciation of taste, in the welding of fifth-nerve or glossopharyngeal tactile, pain, and thermal sensibility with the gustatory stimuli of the chorda, Vidian, or glossopharyngeal nerves, which almost certainly takes place in the cortical centre for taste in the post-central gyrus.

This physiological view I am now putting forward explains the difficulty surgeons and physiologists have had in accepting the idea that the fifth nerve has any share in taste production. Because of the variability of results concerning loss of taste in fifth-nerve lesions the tendency has been to ignore reported cases of loss of taste in fifth-nerve lesions as due to faulty observation.

In view of my results of loss of taste in large numbers of fifth-nerve total lesions, the scheme I have presented seems more than probable.

Conclusions

The large number of cases in which I have tested taste at different intervals of time, after lesions of the fifth nerve have been produced by disease or by alcohol injections of the Gasserian ganglion or its branches, afford definite proof that:

1. Tactile sensibility, including pain and thermal fibres, in the tongue and palate has, in the great majority of persons, an important share in the recognition of taste sensations.

2. In a small minority taste is permanently lost or much diminished in intensity after total fifth-nerve lesions.

3. In the large majority taste is lost on the front of the tongue immediately after such lesions, but returns after intervals varying from a matter of hours, days, weeks, months, or even years, according to the individual degree of dependence on fifth-nerve sensibility.

4. The above three facts prove that the gustatory stimuli provided by the chorda tympani and petrosal nerves are insufficient alone, except in a small minority of persons, to provide full gustatory sensation immediately after a fifth-nerve lesion, but that a dual function of fifth-nerve sensibility together with chorda and petrosal gustatory stimuli is generally required.

5. For the back of the tongue, in the majority of people, taste perception is served by the combined common sensibility and gustatory function of the glossopharyngeal nerve only. In a small minority the tactile and pain sensibility of the back of the tongue is provided, partially or wholly, by the fifth nerve, and taste may be abolished for years in total fifth-nerve lesions.

6. In cases of facial paralysis, if the lesion is at or above the geniculate ganglion, taste is lost not only on the tongue but also on the palate.

7. The palatal loss of taste in these cases of facial palsy is proof that the great superficial petrosal (Vidian) nerve supplies gustatory fibres to the palate, and that their stimuli reach the geniculate ganglion and the pars intermedia via the main palatal nerve and Meckel's ganglion.

8. Taste stimuli reach the medulla and pons via the pars intermedia wrisbergi and the gustatory nucleus, as described by Nageotte, and thence pass by a nerve relay decussating to the opposite side, forming the gustatory fillet, running close to the midline through the pons to the crus, and terminating in the postero-ventral nucleus of the thalamus. Thence the gustatory stimuli are relayed to the lower part of the post-central gyrus in the parietal lobe, immediately behind the motor chewing centre in the pre-central gyrus.

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MASS B.C.G. VACCINATION IN MALTA

REPORT ON THE B.C.G. VACCINATION CAMPAIGN HELD BY I.T.C.* in MALTA IN 1950

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Between March and June 1950, a Norwegian medical team, together with four Maltese medical teams (which the Norwegians trained), carried out a survey of the tuberculin reaction of the section of the population of Malta aged 1–18 years, and vaccinated with B.C.G. the "negative" reactors. The campaign, the first of its kind in Malta, was held on an entirely voluntary basis, and was carried out under the auspices of the I.T.C. under the direction of Dr. A. Weidemann, of Norway, and myself. The tuberculin and B.C.G. vaccine used were prepared at the State Serum Institute in Copenhagen; while the costs were borne mainly by the I.T.C. but in part also by the Government of Malta.

Altogether 48,319 children and youths aged 1–18 years came for testing. The result of 42,986 of these tests is known, while 36,320 were vaccinated with B.C.G.

Of 6,009 persons over 18 years who were tuberculin-tested, 2,361 were vaccinated during the campaign. This report also includes the results obtained in this group.

Reasons for the Campaign

The situation in Malta in respect of tuberculosis can be studied from Table I, which is taken from the 1949 Annual Report of the Chief Government Medical Officer, Malta.

TABLE I.—*Deaths from Pulmonary Tuberculosis in Malta and Gozo*

Year	Estimated Population at End of Year	Cases Notified	Case Rate per 1,000 Population	No. of Deaths	Death Rate per 1,000 Population
1939	269,912	189	0·70	118	0·43
1940	270,755	232	0·86	139	0·51
1941	271,359	294	1·08	178	0·65
1942	269,090	415	1·54	227	0·84
1943	272,121	314	1·15	192	0·70
1944	279,187	261	1·00	146	0·52
1945	286,596	236	0·82	134	0·49
1946	295,247	273	0·92	133	0·48
1947	303,998	220	0·72	161	0·52
1948	304,991*	202	0·66	104	0·34
1949	310,985*	228	0·73	97	0·31

*Mid-year population.

It will be seen that the number of deaths from pulmonary tuberculosis in 1949 was only 97, which gives a rate of 31 per 100,000. As the death rate from other forms of tuberculosis was 12 per 100,000, the total tuberculosis death rate for 1949 was thus 43 per 100,000. It will be agreed that, statistically at least, there was no cause for undue alarm.

Other factors, however, had to be taken into consideration. The 1939–45 war brought about the destruction of a considerable proportion of Malta's habitable dwellings, and the ensuing housing shortage resulted in severe overcrowding in the homes, very large families often being segregated together in small houses of one to three rooms.

Material collected by the tuberculosis home visiting service during 1949 showed that the average tuberculous family consisted of 5.7 persons housed in 2.5 rooms; and that 69% of the patients shared their bedrooms with one to three members of the household, while 17% shared their bed with another member of the family. Of the new cases of pulmonary tuberculosis, 52% preferred domiciliary to hospital treatment.

Finally, the severity of the cases of primary intrathoracic tuberculosis detected in children attending the contacts' clinic could be attributed to the persistent and intimate contact of these children with open cases in a very restricted environment.

All the conditions favouring the spread of the disease certainly existed, and called for the immediate adoption of effective preventive measures. It was recognized that mass B.C.G. vaccination alone would not, indeed could not, solve the whole problem. It was felt, however, that immunization against tuberculosis was the most practical and the speediest weapon with which to combat the conditions created by war. A mass B.C.G. vaccination campaign could allow the nation to tide over the critical period while long-term measures were being developed.

Practical Procedure

An education programme was carried out on the lines of the following principles. Ways and means of public information were devised which most suited local conditions; which gave a true and full picture of the relevant medical facts concerning B.C.G. vaccination; which did not create a nation-wide tuberculophobia, but allowed the people to see the tuberculosis problem in its real perspective; which could reach most of the people most effectively; and which were so spaced and repeated as to keep the interest of the population in B.C.G. vaccination alive throughout the whole campaign.

The island was divided into 42 districts, and each team covered from six to eight of these districts. Each team consisted of one vaccinator, two nurses, and a clerk, and worked in one district for a week. With the co-operation of the education authorities very suitable premises were found in the Government school of each district.

Pre-vaccination Tuberculin Test

For the pre-vaccination tuberculin test the adrenaline-Pirquet (A-P) technique was adopted, mainly because the "Mantoux" necessitated more attendances and the Moro patch test could not be relied upon to give definite and easily interpreted results.

Old tuberculin, of a strength 1.7 times that of the international standard and to which 0.5% phenol had been added during preparation, was used for testing. To each millilitre one drop of 1% adrenaline was added, and every week the adrenaline-tuberculin solution was renewed.

The test is made as follows. The prepared skin of the flexor side of the left forearm is stretched and with a scarificator two scratches 0.5 cm. long and 2–3 cm. apart are made through the epidermis, but preferably neither deep enough to produce prompt bleeding nor too superficial. Adrenaline-tuberculin is rubbed into the two scratches by means of a glass rod, and the arm is kept

*The International Tuberculosis Campaign (I.T.C.) is a joint international effort of: (1) The United Nations International Children's Emergency Fund (Unicef), which furnishes most of the supplies and equipment. (2) The Danish Red Cross, Swedish Red Cross, and Norwegian Relief for Europe, which provide specially trained physicians and nurses. (3) The World Health Organization (W.H.O.), which sets standards, provides technical advice and assistance, and evaluates the results. (4) The Ministry of Health of the country in which a campaign is being conducted, which provides local supplies, facilities, and medical teams.

uncovered for 5 minutes, after which any tuberculin remaining can be wiped off.

The test is read after 72 hours, the infiltration being measured across the scratches at the point where the reaction is strongest. The higher of the two figures is recorded and any vesiculous reaction or lymphangitis present noted. The reaction is considered "positive" when the infiltration definitely measures 3 mm. or more.

Complications of the Test

In the "positive" reaction the induration varied from 3 to 22 mm., though most reactions were from 4 to 9 mm. in size.

Vesiculation occurred in 97 individuals, whose ages ranged from 1 to 18 years and whose reaction measurements ranged from 5 to 12 mm.

Lymphangitis was reported in 102 individuals, whose ages varied from 4 to 18 years and whose reaction measurements ranged from 5 to 17 mm.

Secondary infections with pyogenic micro-organisms were found in 27 cases.

Dispersed local reaction was found in 15 cases. During testing the tuberculin solution had accidentally soiled the rolled-up shirt-sleeve, which, acting in the manner of a percutaneous test, produced this "positive" reaction.

Febrile Reaction.—Five children between 6 and 15 years old complained of a mild fever (99–101° F.—37.2 to 38.3° C.) for one to three days after the test. Three of these had a "clear" chest skiagram, while calcifying hilar nodes were noted in two, one having in addition a calcified spot (Ghon) in the right lower zone.

Erythema Nodosum.—A girl aged 5 years, giving a 13-mm. "positive" tuberculin reaction, developed a nodular eruption three days after the test. Her chest skiagram showed an adenitis in the left hilum with collapse of the left upper lobe. On contact investigation her father was found to be suffering from open pulmonary tuberculosis.

Erythema Multiforme.—The following typical case was confirmed by a skin specialist. It is natural to ask whether the tuberculin test might have precipitated the eruption, especially in view of the known aetiological relationship of drugs, sera, etc., to this condition.

A married woman aged 37, with a healthy past and family history, was tuberculin-tested on May 3, 1950, on the volar aspect of the left forearm. That same evening she developed an intense itching and redness on the dorsal aspect of the left hand. She applied some balsam locally and bandaged her hand. Next day she developed a rash affecting her forehead, face, and neck as well as her forearms and legs. The eruption came out all at once and in no definable order. No itching was complained of.

On examination her temperature was 99° F. (37.2° C.), pulse 78, and respirations 18. No abnormality was detected on examination of the lungs, heart, abdomen, and central nervous system. The urine contained no abnormal elements. A blood count showed: red cells, 5,000,000; haemoglobin, 84.2 g.%; colour index, 0.9; white cells, 19,000 (polymorphs 78%, lymphocytes 22%). A skiagram of the chest revealed calcified foci in the left lung; no evidence of any active lesion. The Wassermann reaction was negative. The rash consisted of large discrete raised papulo-vesicles, circular or oval in shape. Each of these was set on a more diffuse erythematous base and exhibited a central depression and centrifugal radiations. The rash was bilateral and roughly symmetrical, and on the whole was confined to exposed parts. All the mucous membranes accessible to inspection were healthy. The local reaction to the tuberculin test appeared in every way a normal one. There was no evidence of vesiculation, lymphangitis, or secondary infection.

Results

Roughly 85% of the results read were "negative," while the incidence of infection in the first 15 years of life was practically identical in the two sexes (Table II). In the last three age groups (16 to 18 years), however, there was a steady tendency for the proportion of "positive" male reactors to exceed the female one. This tendency continued in the groups aged 19 to 20 years (years of birth, 1931–30), as may be seen from Table III. (This table deals with 5,933 cases, 76 of the 6,009 being unavailable for analysis.)

It is probable that these differences are a reflection of the fact that Maltese lads aged 16 to 20 are more likely than

TABLE II.—*Results of Tuberculin-testing*

Age in Years	Year of Birth	No. Tested	No. Read	Results Known	Positive Reactors	Negative Reactors
Males						
1	1949	818	119	699	13 (1·8%)	686 (98·2%)
2	1948	1,590	239	1,351	28 (2·1%)	1,323 (97·9%)
3	1947	1,785	232	1,553	52 (3·4%)	1,501 (96·6%)
4	1946	1,731	216	1,515	75 (4·9%)	1,440 (95·1%)
5	1945	1,861	222	1,639	78 (4·7%)	1,561 (95·3%)
6	1944	1,777	201	1,576	100 (6·4%)	1,476 (93·6%)
7	1943	1,293	139	1,154	94 (8·2%)	1,060 (91·8%)
8	1942	1,094	116	978	111 (11·4%)	867 (88·6%)
9	1941	1,172	126	1,046	155 (14·8%)	891 (85·2%)
10	1940	1,450	148	1,302	209 (16·1%)	1,093 (83·9%)
11	1939	1,487	156	1,331	272 (20·5%)	1,059 (79·5%)
12	1938	1,668	179	1,489	355 (23·8%)	1,134 (76·2%)
13	1937	1,501	156	1,345	315 (23·5%)	1,030 (76·5%)
14	1936	1,458	187	1,271	360 (28·4%)	911 (71·6%)
15	1935	1,020	132	888	262 (29·5%)	626 (70·5%)
16	1934	770	104	666	242 (36·4%)	424 (63·6%)
17	1933	645	108	537	207 (38·5%)	330 (61·5%)
18	1932	532	78	454	200 (44·1%)	254 (55·9%)
		23,652	2,858	20,794	3,128 (15·1%)	17,666 (84·9%)
Females						
1	1949	782	112	670	11 (1·5%)	659 (98·5%)
2	1948	1,571	213	1,358	42 (3·1%)	1,316 (96·9%)
3	1947	1,728	203	1,525	38 (2·5%)	1,487 (97·5%)
4	1946	1,723	179	1,544	58 (3·7%)	1,486 (96·3%)
5	1945	1,762	179	1,583	101 (6·4%)	1,482 (93·6%)
6	1944	1,803	179	1,624	109 (6·7%)	1,515 (93·3%)
7	1943	1,325	147	1,178	114 (9·6%)	1,064 (90·4%)
8	1942	1,122	107	1,015	97 (9·5%)	918 (90·5%)
9	1941	1,171	116	1,055	130 (12·4%)	925 (87·6%)
10	1940	1,580	139	1,441	223 (15·5%)	1,218 (84·5%)
11	1939	1,559	132	1,427	263 (18·5%)	1,164 (81·5%)
12	1938	1,620	140	1,480	288 (19·5%)	1,192 (80·5%)
13	1937	1,490	126	1,364	324 (23·7%)	1,040 (76·3%)
14	1936	1,432	140	1,292	351 (27·2%)	941 (72·8%)
15	1935	1,099	96	1,003	289 (28·8%)	714 (71·2%)
16	1934	1,092	99	993	304 (30·6%)	689 (69·4%)
17	1933	959	82	877	292 (33·3%)	585 (66·7%)
18	1932	849	86	763	292 (38·3%)	471 (61·7%)
		24,667	2,475	22,192	3,326 (15·0%)	18,866 (85·0%)

It is probable that these differences are a reflection of the fact that Maltese lads aged 16 to 20 are more likely than

TABLE III.—*Result of Tuberculin-testing 5,933 Persons Over 18 Years Old*

Year of Birth	Males			Females		
	Tested	Positive	Negative	Tested	Positive	Negative
1931	209	102 (48·8%)	107 (51·2%)	392	154 (39·3%)	238 (60·7%)
1930	154	80 (51·9%)	74 (48·1%)	366	168 (45·9%)	198 (54·1%)
1929/25	536	362 (67·5%)	174 (32·5%)	1,234	626 (50·7%)	608 (49·3%)
1924/20	341	271 (79·4%)	70 (20·6%)	931	522 (56·1%)	409 (43·9%)
1919/15	190	156 (82·1%)	34 (17·9%)	534	335 (62·7%)	199 (37·3%)
1914/10	153	135 (88·2%)	18 (11·8%)	432	290 (67·1%)	142 (32·9%)
1909/05	86	78 (90·6%)	8 (9·4%)	217	153 (70·5%)	64 (29·5%)
1904/00	49	43 (87·7%)	6 (12·3%)	109	78 (71·5%)	31 (28·5%)
Total ..	1,718	1,227 (71·4%)	491 (28·6%)	4,215	2,326 (55·2%)	1,889 (44·8%)

girls of that age to have left the relatively sheltered life of their homes and to be engaged in occupations entailing a wider contact with the community.

Some of those infected with tubercle bacilli eventually develop tuberculosis, and, since more cases of phthisis had been occurring among males than among females of the age group 16 to 20, one had expected that more males would also be found infected than females in this group. The results of the campaign confirmed this expectation.

On the other hand, since the incidence of phthisis was in actual fact higher in the male, one would have expected a higher male mortality in this age group, or at least in the next group (20–25). Contrary to expectation, in the period 1944–50 there were many more female deaths than male in both age groups. It seems, therefore, that at ages 16–20 more males than females are infected with tubercle bacilli and in consequence more males develop pulmonary tuberculosis, which, however, is less likely to progress to a fatal issue than in the female.

District Analysis of Results

For the purposes of this investigation the districts covered during the campaign were divided into 14 rural, 10 semi-rural, 11 suburban, and 7 urban areas (Table IV).

TABLE IV.—*Results of Tuberculin-testing in Four Types of Districts*

Districts	Total Population	Population Aged 1–18			Incidence of Pulm. Tub. per 1,000 Population
		No.	% Tested	% Positive Reactors	
Rural (14) ..	38,125	15,503	40·9	8·6	0·22
Semi-rural (10)	79,555	31,178	31·1	14·0	0·51
Suburban (11)	92,881	37,178	41·8	16·7	0·66
Urban (7) ..	68,550	25,201	37·1	20·0	0·61

This district analysis has shown that the incidence of tuberculous infection and of pulmonary tuberculosis is decidedly lower in the rural areas than in any other part of Malta, and that in the semi-rural, suburban, and urban areas conditions are approximately identical.

B.C.G. Vaccination

Immunization was carried out by means of Wallgren's intradermal injection technique, in preference to the scarification method of Bretey and to Rosenthal's multipuncture method, chiefly because it was felt that the method chosen was the only one that allowed the dosage to be measured with accuracy and therefore to be standardized.

The following is a description of the vaccination technique used during the present campaign. The ampoule containing the vaccine is shaken vigorously in order to ensure an even suspension of the bacilli. Then 0.1 ml. of the vaccine is aspirated in a 1-ml. syringe, and through a very small platinum-iridium needle (No. 20) it is injected intradermally into the skin overlying the left deltoid. After a correct injection a 10-mm. wheal forms, in which the hair follicles stand out prominently. The vaccine supplied by the State Serum Institute of Copenhagen contains 0.025 mg. of B.C.G., or about 1 million "B.C.G. bacilli," per 0.1 ml. The number of persons vaccinated is shown in Table V.

The Reaction to B.C.G. Vaccination

Briefly, the events following vaccination are: (1) the development of a primary focus at the site of inoculation through the multiplication of the bacilli injected; (2) lymphogenic spread of the process to the regional glands; (3) haematogenous dissemination of the bacilli to distant organs and probably their partial elimination in the urine; (4) the development of allergy after an incubation period of three to four weeks.

The local changes vary. Normally the small wheal made by the intradermal injection of the vaccine disappears within

TABLE V.—*Number of Persons Vaccinated with B.C.G.*

Year of Birth	Negative Reactors			B.C.G. Vaccinations		
	Males	Females	Total	Males	Females	Total
Aged 1–18:						
1949	686	659	1,345	672	650	1,322
1948	1,323	1,316	2,639	1,304	1,295	2,599
1947	1,501	1,487	2,988	1,480	1,473	2,953
1946	1,440	1,486	2,926	1,428	1,478	2,906
1945	1,561	1,482	3,043	1,555	1,470	3,025
1944	1,476	1,515	2,991	1,468	1,502	2,970
1943	1,060	1,064	2,124	1,058	1,059	2,117
1942	867	918	1,785	863	913	1,776
1941	891	925	1,816	889	922	1,811
1940	1,093	1,218	2,311	1,091	1,216	2,307
1939	1,059	1,164	2,223	1,058	1,161	2,219
1938	1,134	1,192	2,326	1,131	1,191	2,322
1937	1,030	1,040	2,070	1,026	1,039	2,065
1936	911	941	1,852	909	939	1,848
1935	626	714	1,340	625	712	1,337
1934	424	689	1,113	422	685	1,107
1933	330	585	915	329	583	912
1932	254	471	725	253	471	724
Total	17,666	18,866	36,532	17,561	18,759	36,320
Over 18:						
1931	107	238	345	107	237	344
1930	74	198	272	73	196	269
1929/25	174	608	782	172	604	776
1924/20	70	409	479	70	407	477
1919/15	34	199	233	33	197	230
1914/10	18	142	160	18	139	157
1909/05	8	64	72	8	63	71
1904/00	6	31	37	6	31	36
Total ..	491	1,889	2,380	487	1,874	2,361

10–30 minutes, and for some time thereafter nothing is seen at the site of inoculation. At the end of three to four weeks a red nodule appears, which may or may not become a small pustule or, following the discharge of the pus, a tiny ulcer. Finally after a variable interval scarring occurs.

The variations in the local reaction to vaccination are to a large extent due to variations in the natural resistance of persons vaccinated as well as to differences in dosage and technique of administration of the vaccine. In order to minimize the risk of abscess formation locally and in the draining regional glands, during the campaign great stress was laid on the importance of: shaking the ampoules to avoid clumps of bacilli, checking the dosage (0.1 ml.) during each inoculation, and avoiding subcutaneous inoculation.

Koch Phenomenon

An accelerated reaction at the site of inoculation may follow the vaccination of those already infected with tubercle bacilli. This premature abnormal reaction, known as the Koch phenomenon, is to be expected in a mass campaign, since no known tuberculin test can be relied upon to detect 100% of those already infected.

In order to check its incidence during this campaign and to ascertain the characters of the local reaction within the first week of immunization, various unselected groups of vaccinated individuals were examined quite soon after vaccination.

TABLE VI.—*Results of Examination of Local Reaction to B.C.G. Vaccination*

Day After B.C.G. Vacc.	Total No. of Exams.	Age Group in Years	Size of Infiltration		Size of Erythema		No. Having Pustule	No. Showing Koch Phen.
			0–8 mm.	9–12 mm.	8–10 mm.	10–20 mm.		
3rd	268	6–16	267	1	260	8*	9	1
4th	541	6–19	541	—	534	7	4	—
5th	261	6–16	260	1	256	5	1	—

* Of these, one had a 35-mm. erythema.

The presence of a pustule so soon after vaccination was puzzling. Its cause could not be determined with any certainty. It is possible that these pustules were being produced by a mild secondary infection of the site inoculated, in spite of the fact that the hypodermic needles used for the intradermal injection of the vaccine were made red-hot immediately before each vaccination.

Throughout the whole campaign 11 cases of Koch phenomenon were referred to me. The commonest finding was a darkish circular ulceration with a tendency to sloughing at the site of vaccination three to six days after inoculation. Other findings included: (1) a "positive" tuberculin reaction in the test-scratches which before vaccination had given a "negative" reaction; (2) enlargement of lymph nodes in the axilla on the side of vaccination unaccompanied by enlargement of other groups of palpable glands; (3) fever ranging from 99 to 102° F. (37.2 to 38.9° C.) accompanied by chilliness, malaise, and headache; and (4) *x*-ray evidence of healed or active tuberculosis. Clinical and *x*-ray supervision of these cases has not revealed any complication in any of them.

Ulcers and Local Abscesses

In all, 23 cases of discharging ulcer were referred to the clinic. The condition tended to appear between the 30th and 53rd days after vaccination. The ulcers were usually punched out, were between 13 and 37 mm. in diameter, and were discharging greenish purulent matter. On the whole the ulcers tended to heal rapidly, but it was difficult to ascertain the duration of the discharge because in many cases the scab formed was scratched away and the purulent secretion started all over again. In two cases fever and constitutional symptoms were noted. Oral administration of para-aminosalicylate (8 to 10 g.) to these cases brought about an improvement in the local and general conditions within two to three weeks.

Secondary infection was definitely a contributory factor in several of these cases, which healed rapidly after the local application of a sulphonamide powder thrice daily, the area being covered during the day with gauze soaked in acriflavine solution 1/1,000.

Glandular Reaction

We did not consider glandular enlargement to be a complication of B.C.G. vaccination unless it accompanied suppuration at the site of vaccination, caused pain or discomfort or limitation of movement of the arm, or the adenitis showed a tendency to suppurate. Of the 54 cases referred to us for glandular enlargement in the axilla following B.C.G. vaccination, two had a secondarily infected B.C.G. ulcer, two complained of discomfort on movement, while in 21 cases the condition progressed to suppuration.

This complication occurred in 13 boys and 8 girls aged 1–6 years, and 17 of the 21 were between 2 and 3 years old. It will be seen, therefore, that it showed a marked tendency to occur in very young children. Of the 5,552 aged between 2 and 3 years 17 developed a glandular abscess after vaccination; and of 15,775 children aged 1–6 years 21 developed a suppurative adenitis.

In all the cases the local reaction to B.C.G. vaccination consisted of a small (4–7 mm.) ulcer discharging greenish purulent matter. A second tuberculin test revealed a "positive" reaction with an infiltration varying between 5 and 8 mm. The interval between vaccination and the appearance of an axillary lump varied between two and four months. The adenitis became suppurative in a further one to three months. All these glandular reactions without exception occurred on the side of vaccination. The abscess developed in the anterior axillary fold in 13 cases and in the mid-axilla in four cases. Three children had a supraclavicular abscess and one boy an infraclavicular one. The constant rubbing of the skin by tight clothing overlying abscesses at the anterior axillary fold precipitated rupture of the abscess. Most of these children developed a secondary anaemia with mild leucocytosis during the period of suppuration. Two cases had fever and loss of appetite for a few days, but these symptoms subsided quickly after rupture of the abscess. Chest skiagrams were taken of all the cases. No abnormal intrathoracic glandular reaction was detected.

Oral administration of para-aminosalicylate, 8 g. a day, in 10 cases did not seem to affect materially the progress of the adenitis towards suppuration. When fluctuation was noted these abscesses were aspirated through adjacent healthy skin. In some cases this was followed by a sinus formation or by re-formation of the abscess. From 2 to 10 ml. was aspirated at one sitting. The purulent matter extracted was examined and acid-fast bacilli were seen microscopically. In none of the cases was secondary infection detected. When these abscesses burst or formed a sinus, a sulphonamide powder and para-aminosalicylate were applied thrice daily and the site was protected with gauze soaked in 1/1,000 acriflavine solution. At the time of writing (10–14 months after vaccination) 12 cases have ceased to discharge and have formed a scar.

Scar

It has not been possible to give the exact number of people whose reaction to vaccination has been examined 6–10 months after the inoculation. The group, however, includes several hundreds, and in most of them a scar has formed. Its size varies from 4 to 15 mm. It is usually circular, being purplish in colour peripherally and thin and translucent at the centre. In a very small minority of those seen a scab is still present at the site of vaccination.

Post-vaccination Tuberculin Test

Very extensive experience with the vaccine had proved it capable of achieving a 98–99% conversion rate. To check the efficacy of both the vaccine and the technique of its administration, 2,421 unselected vaccinated individuals were tested. In 1,975 (98.95%) of these the result was "positive" and the size of the reaction obtained varied between 3 and 10 mm.; while in 21 persons (1.05%) aged between 1 and 17 years, of whom four were 5 years and four were 11, the results obtained were "negative" as follows: 6 with a 0-mm. reaction, 3 with an infiltration of 1 mm., and 12 with a 2-mm. reaction.

In order to gain experience in the matter of revaccination an effort was made to find and follow-up as many post-vaccination "negative" reactors as possible. Instead of revaccinating these, they were followed up with A-P tests every four weeks to see if and when conversion would eventually take place. Eight cases of this nature which were followed up for three to six months eventually did give a "positive" (3–5 mm.) reaction. It is possible, therefore, that conversion does not always occur as promptly as one would expect, and that eagerness to revaccinate too soon after a post-vaccination "negative" tuberculin reaction may be unjustified in at least some cases.

In 367 post-vaccination "positive" reactors, periodic retesting over a period of six months with the A-P technique failed to show any significant increase or decrease in the size of the reaction to the test.

Finally, 17 persons who were known to be "tuberculin-negative" six months after vaccination were subjected to the B.C.G. diagnostic test described by Ustvedt and Aanonsen (1948). With a gramophone-needle-holder two intradermal punctures were made through a drop of B.C.G. vaccine. Two to four days after the test 11 of the cases developed a local darkish reaction, which in three proceeded to ulceration. The result resembled a Koch phenomenon. In two cases a transient erythema was noted locally, but nothing else eventually developed; while in another four cases the result two to three weeks after the test was similar to that obtained after a normal B.C.G. vaccination.

It is Ustvedt's opinion that the early reaction that occurred in 11 of the cases is one denoting that the previous B.C.G. vaccination had successfully infected these individuals despite the repeatedly "negative" A-P tuberculin tests. It is quite probable that this diagnostic B.C.G. test is more sensitive and specific than the A-P test and therefore eminently suitable for application on post-vaccination "negative" reactors. In view of the limited size of this experiment the conclusion reached must be regarded only as a tentative one.

X-ray Examination of Positive Reactors.—Mass *x*-ray examination of "positive" reactors could not, however, be considered owing to the lack of a mass radiography apparatus in Malta. Those in charge of the tests were asked to give priority to the following: (1) young "positive" reactors aged 1–3 years; (2) members of families in which the incidence of "positive" reactions in the children suggested the presence of a source of infection in the home; and (3) "positive" reactors who complained of ill-health or suspicious symptoms.

Complications in B.C.G. Vaccination Subjects

Febrile Syndromes

Considering the universal tendency to regard in the light of cause and effect every medical ailment occurring after vaccination, the number of cases of fever after B.C.G. immunization that have been referred to us are surprisingly few. In some the fever could be attributed to a severe local reaction, and these cases have already been mentioned. Others in whom the local reaction was quite normal complained of fever accompanied by malaise and decreased energy, or lack of appetite and loss of weight. These symptoms had come on one to four weeks after vaccination and lasted from a few days to a few weeks.

Systematic clinical inquiry, physical examination, diverse laboratory examinations, and chest *x*-ray examination were carried out in each case. Only in three or four cases could the suspicion of a specific B.C.G. effect be entertained. In these no plausible explanation for the fever could be found.

Allergic Syndromes

These include one case of erythema nodosum and 17 cases of phlyctenular conjunctivitis.

Erythema Nodosum.—A girl aged 7 was vaccinated with B.C.G. following a 0-mm. "negative" tuberculin reaction. Twenty-nine days later she developed typical erythema nodosum. One brother and two sisters had also been vaccinated. All the members of her family had a "chest clear" *x*-ray report. Her parents denied any family history of tuberculosis. The post-vaccination tuberculin reaction was "positive" (4 mm.). She had a clear chest *x*-ray film and no past history of similar rashes or of sore throat or tonsillitis, etc. Inspection of her throat did not reveal any abnormality. Throat swabs showed no haemolytic streptococci. The E.S.R. was 5 mm. in the first hour. Fever ranged from 99 to 101° F. (37.2 to 38.3° C.).

This case is interesting, and raises the question whether erythema nodosum can occur as a pure B.C.G. effect.

Phlyctenular Conjunctivitis.—I am indebted to Dr. F. Damato and Dr. V. Tabone for the following particulars.

Dr. Tabone writes: "I have seen six cases of phlyctenular conjunctivitis following B.C.G. vaccination. In most cases the conjunctivitis came on two to three weeks after vaccination; it ran the usual course, and all cases cleared up eventually on the usual treatment (mainly symptomatic). It appears that during the building of specific antituberculous immunity there can be an allergic ocular manifestation with the production of the phlyctenules."

Dr. Damato writes: "I saw 11 cases of phlyctenular conjunctivitis and keratitis in children vaccinated with B.C.G. Their ages varied between 4 and 8 years. A chest *x*-ray film was taken in all these cases: none showed signs of infiltration; enlargement of hilar glands was the only finding. The number of phlyctens was usually one. Subjective symptoms were rather marked; were it not for this fact the children would never have been brought for examination. All cases responded very well to treatment by sulphacetamide 30% instilled three-hourly and ung. hydrargyri oxidi flavi applied twice a day, and cod-liver oil by mouth. There was no recurrence of the ophthalmia."

As Dr. Damato pointed out to me, these cases are interesting because they constitute some evidence against an ectogenous origin of the condition and would seem to confirm the view that the phlyctens are an allergic manifestation of tuberculous infection even when this is as mild as that produced by B.C.G. vaccination.

Vaccination in Pre-allergic Phase

A female nurse aged 23 was vaccinated with B.C.G. on March 17, 1950, after a 0-mm. "negative" tuberculin reaction. Before vaccination she had been working in an orthopaedic ward where cases of surgical tuberculosis were admitted. About March 30 she began to get easily tired, to lose her appetite, and to feel feverish. She eventually reported sick on April 20. On examination she looked tired, had a temperature of 100° F. (37.8° C.), and her chest skiagram revealed an active adenitis in the left hilum but no pulmonary lesion. She now gave a "positive" tuberculin reaction (9 mm.). She was kept in bed and *x*-rayed every two to four weeks, and was on a sanatorium regime. Her temperature subsided and her general condition improved. She is still under observation, and serial *x*-ray examinations show regression of the hilar lesion. This case is important because she appears to have been inoculated with B.C.G. while in the pre-allergic phase of the adenitis. Convalescence was rapid and uneventful, and vaccination does not seem to have affected the condition, which on the whole has been quite benign.

Tuberculous Disease

The Tuberculosis Control Section, to which all forms of tuberculosis are notified, made it a point of inquiring, in every case notified since the campaign started, whether or not the patient had been vaccinated with B.C.G. Up to 12–15 months after the campaign none of the cases of tuberculosis that have been reported had been vaccinated with B.C.G.

Comments

Certain points connected with the investigation require further comment.

(1) *Age Limit.*—We did not include infants less than 1 year old, because their immunogenic powers are limited and many would have required revaccination, and because their very thin skin would have made intradermal inoculations difficult and many a local abscess would have resulted from too deep an injection of the vaccine.

(2) *Isolation.*—At its meeting in Paris on June 15, 1948, the W.H.O. Subcommittee on Tuberculin Testing and B.C.G. Vaccination recommended: "That for the mass-vaccination programme isolation of vaccinated persons was not necessary, and that segregation of open cases, even though desirable for other reasons, is considered not to be an essential measure for a mass B.C.G. vaccination programme." In view of these recommendations isolation of vaccinated contacts with open cases of tuberculosis was not carried out, though, whenever possible, infectious subjects were asked to keep away from their homes for at least a few weeks either by entering hospital for treatment or by seeking other accommodation temporarily.

(3) *Follow-up.*—Plans have been devised for the future follow-up of all the cases vaccinated. It is further proposed to hold regular campaigns of this nature. It is also intended to offer vaccination to all contacts, nurses, and medical students, and to patients suffering from diabetes mellitus. Unicef has provided us with the necessary transport and with clerical and medical equipment, and thus made possible the fulfilment of these plans.

(4) *The difficulties* we have encountered were: those arising from the need of adapting general principles and procedures to suit local customs and conditions, and those created by prejudices and fears which are the almost inevitable accompaniment of any new venture.

(5) *The impressions* we have formed are: (1) that it is possible by factual, sober propaganda to obtain that degree of public response which justifies the effort and expense involved in such a campaign; (2) that valuable information may be obtained by relating the results of the tuberculin

tests to other data collected from the clinical and administrative control of tuberculosis; (3) that the adrenaline-Pirquet test is harmless, reliable, and easily applied, and gives straightforward results; (4) that B.C.G. vaccination is harmless; it is very rarely attended by complications, and these are on the whole quite benign; (5) that if reliable information is to be obtained the follow-up of those vaccinated should be centralized both clinically and administratively.

(6) *Tuberculosis control* has benefited from the campaign in three main ways. First, it has stimulated in the public a healthy interest in tuberculosis; secondly, the age, sex, and district analyses of the results of tuberculin-testing have given us a fairly clear picture of the way tuberculous infection is affecting the community; finally, through B.C.G. vaccination we have conferred on 40% of our younger generation a degree of protection from tuberculous disease which they could not, with equal safety, have otherwise secured.

It is for the future to show us not only the duration of the immunity we have conferred but also: (1) whether in Malta, by comparing the incidence of tuberculosis before and after the present campaign, further evidence can be obtained that B.C.G. vaccination is in reality the effective preventive measure we now believe it is; and (2) whether, by comparing the incidence of tuberculosis in those vaccinated with B.C.G. and in those unvaccinated, it can be shown that B.C.G. offers efficient protection from tuberculous disease, as we now believe it does.

Summary

Between March and June, 1950, 54,328 persons in Malta were tuberculin-tested and 38,681 were vaccinated with B.C.G. The reasons for this campaign and the methods of its actuation are given.

The tuberculin-testing results are subjected to age, sex, and district analyses; while the results of vaccination, together with the local reactions seen and the complications encountered, are described.

The methods adopted for following up the campaign, such as the retesting of those vaccinated and the *x*-ray examination of selected groups of initially "positive" reactors, are included.

It would not have been possible to carry out this campaign but for the generosity of the I.T.C. Organization, which, in addition to sending a skilled team, supplied all the necessary equipment, tuberculin, and vaccine, and, together with the Malta Government, bore all the expenses involved. I am indebted to all who took part in the campaign and particularly to the teams so ably led by Dr. A. Weidemann, I.T.C. Chief of Mission, and his Norwegian staff. I wish to thank the Chief Government Medical Officer and his staff for their valuable administrative help; Dr. H. J. Ustvedt for his interest and advice; Miss Nordahl, of W.H.O., for her statistical work; and Miss C. Busuttil and Mr. J. R. C. Agius, of this department, for their help during the campaign and in the preparation of this paper. My thanks are also due to Professor A. C. Briffa, Chief Government Medical Officer, Malta, for permission to publish this paper.

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The Canadian National Research Council is supporting investigations for devising artificial hearts, reports the division of medical research. Three workers at the Sick Children's Hospital, Toronto, have built an artificial heart, designed to shunt the blood from the heart of a child suffering from congenital heart disease while the surgeon is repairing the heart. In their preliminary work they have demonstrated that the instrument may safely be used in surgery. The council has made 10 other grants to medical scientists to investigate various phases of cardiac failure.

GALL-STONES: A CLINICAL SURVEY

BY

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Gall-stones have been recognized as a clinical entity for several hundred years. Indeed, Robertson (1945), in an exhaustive review of the historical aspect, quotes a publication by Benevenius dated 1506 on gall-stones, very aptly entitled *On the Hidden Causes of Disease*. Although we have progressed some distance since those early days, gall-bladder disease still remains an unsatisfactory chapter, containing far too many loose ends.

Aetiology

Davidson (1944) discusses the aetiology of cholecystitis and cholelithiasis, and states that a considerable diversity of opinion exists about the relative significance of the various possible causative factors. Weiss (1944) suggested that there is probably a hereditary predisposition to cholelithiasis; the anamnesis frequently reveals that members of several generations show the disease or that several siblings suffer from it. The same writer also mentions the patient's mode of life (sedentary habits), tight garments (corsets and belts constricting the abdomen and checking the flow of bile), infectious diseases (typhoid, pneumonia), dietary indiscretions, and pregnancy—the well-known so-called predisposing factors. As an explanation Weiss suggested that there may be a hereditary disturbance of cholesterol metabolism in the gall-stone patient, but Davidson in the same year stated that there is no proof of any general metabolic defect in cholesterol metabolism, but suggested that some other factor, such as infection, is needed to bring about the precipitation of cholesterol or pigments in the form of gall-stones. It seems to be more generally agreed that a sedentary life and an unbalanced diet play an essential part. Commenting on the well-recognized high incidence of gall-stones in the middle-aged and elderly, Davidson suggests that failing function and decreased efficiency in certain essential functions of the liver and gall-bladder are also probable factors.

But more recent work on steroid metabolism tends to support the views of Weiss, that a fundamental disturbance in cholesterol metabolism may be the principal factor in gall-stone production. Hitherto unknown disturbances of steroid metabolism have recently been recognized in another quite distinct disorder, and may well prove to be of great significance in its aetiology: we refer to rheumatoid arthritis. Sommerville *et al.* (1950) demonstrated that rheumatoid arthritics of both sexes excrete an unusually high proportion of intramuscularly injected progesterone in the urine as pregnanediol, a finding supported later by Copeman *et al.* (1950).

Cholesterol is a constituent of every cell in the body; like progesterone it is a steroid, although little is known about its site of origin, function, or metabolism (Davidson, 1944). It is well known that large amounts of cholesterol are present in most gall-stones, and that the highest concentration of the steroid is to be found in the suprarenal glands. There is a known association between pregnancy and cholelithiasis (Weiss, 1944), and we also know that the sex incidence and age incidence of this disease run closely parallel with those of rheumatoid arthritis, in which abnormal steroid metabolism is known to occur. It is not, perhaps, stretching imagination too far if we press the analogy between the two diseases and suggest that abnormal steroid metabolism may be the basic factor in the lithogenous process. A virtue of this

theory is that it would help to explain the definite clinical association of obesity, sex and age incidence, parity, and hereditary predisposition with cholelithiasis. It would appear that steroid metabolism is more likely to become unbalanced in females as a result of either pregnancy or advancing years.

Symptomatology

Mentzer (1932) observed that the clinical diagnosis of cholecystic disease is far from simple. The predominating impression gained from the average textbook account of symptoms is one of vagueness, in sharp contradistinction to the symptomatology of peptic ulcer. It was the search for a guiding star that led to the present investigation. We felt that gall-stones were being discovered too often accidentally, as the result of an investigation undertaken when everything else was negative. And the converse was only too bitterly true—normal cholecystograms in our imagined "typical history."

Jordan (1948) attempted to clarify the symptomatology by differentiating two groups of patients: (1) those with definite attacks of typical pain and associated symptoms, who remain symptom-free between attacks; and (2) those who are almost constantly disturbed by chronic dyspepsia—constipation, transient attacks of diarrhoea, migratory abdominal cramp-like pains, postprandial distension, and flatulence. These multifarious symptoms are usually grouped as "gall-bladder dyspepsia," and we have adhered to this time-honoured terminology though it is completely misleading. All that such symptoms denote is disordered alimentary function, and it is the all-too-common belief that they directly point the finger of sin at the gall-bladder. When careful investigation proves the innocence of that organ we are disappointed, if not actually annoyed; our proposed victim has eluded us, and another will not be easy to find.

It is impossible to deny that on occasion chronic disease of the gall-bladder can produce alimentary dysfunction by interference presumably with the peristaltic gradient in the stomach and bowel, on the analogy of the severe "dyspepsia" which can undoubtedly be caused by relapsing appendicular disease. But the latter syndrome is not common, and it is our firm belief that true gall-bladder dyspepsia is not common either. Cholecystectomy for gall-bladder dyspepsia is highly unfruitful: the patient loses her gall-bladder but not her symptoms. The unsuccessful results of surgery for dyspepsia without colic do not, of course, prove that the gall-bladder is not at fault, but unfortunately this organ is only a moiety of the biliary system, and some focus for reflex disturbance may well be left. And there is also the unfortunate fact that an organ long habituated to disordered function relinquishes its bad habits most reluctantly. However, our basic tenet here is that relatively few stout middle-aged women with a flatulent dyspepsia have cholecystitis, with or without gall-stones.

In an analysis of over 1,000 cases of cholelithiasis confirmed at operation, Adams and Stranahan (1947) noted that pain was the predominant symptom, being present in 93% of cases. Detailed descriptions of the colic associated with gall-stones have been published by Weiss (1944), Adams and Stranahan (1947), and McKell (1948). The present study embraces 100 cases, and we have found it helpful to define more than one type of pain associated with gall-stones. Many of our patients did not describe attacks of excruciating colic localized to the right upper abdomen and epigastrium with the typical radiation to the inferior angle of the right scapula. In 50% of our series patients described a pain, often sharply localized, in the right hypochondrium, variously described as a severe discomfort or as a particularly unpleasant aching pain. These symptoms occurred in attacks lasting from half an hour to four hours, and were often not accompanied by "gall-bladder dyspepsia," the commonest associated symptom being vomiting. Our impression was that this latter type of attack constituted a fairly precise clinical entity, particularly when seen in the classical type of patient. These people seldom had textbook biliary colic. We endeavoured, therefore, to differentiate our material into two groups, which we labelled "major colic" and "minor colic," analogous with major and minor epilepsy. We were also impressed with the frequency with which the pain was nocturnal—a fact noted by McKell, who observed that most patients will have been awakened at night: it is not only the duodenal ulcer which awakens at night. In fact, many of our patients experienced pain only in the late evening or during the night, and were symptom-free throughout the day (see below).

Nausea and vomiting are the next most prevalent symptoms, occurring in 65% of the cases analysed by Adams and Stranahan. When faced by a patient with minor colic accompanied by gall-bladder dyspepsia it is the first duty of the clinician to determine so far as is possible whether the general dyspeptic symptoms are part and parcel of the cholecystic disease. Unfortunately, this is usually impossible, though a barium meal is often well worth while to exclude additional pathological conditions, such as peptic ulcer or hiatus hernia. Many patients with flatulent dyspepsia and vague abdominal cramps are fundamentally neurotic and constitutionally inferior, and if this type of make-up is unsuspected surgery will do little except remove gall-bladder colic and prevent complications. The "irritable colon" is a deeply rooted syndrome in these unfortunates, and is notoriously resistant to medical guile. In other words, we must be aware of what surgery can do, and accept with gratitude, and not expectation, if it does anything more.

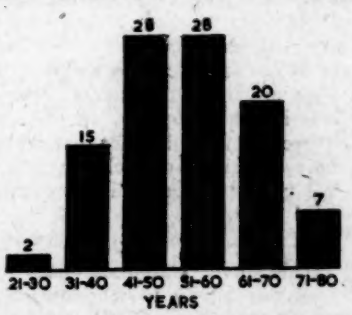
It is an obvious corollary that in the diagnosis of gall-stones little attention should be devoted to such symptoms as belching, flatulent distension, aversion to fatty food, and nausea. It is real pain which should be sought for in the history and made the cornerstone of diagnosis. We stress this because we feel that much current teaching leads the medical student astray and implants ideas which time and experience do not always remove. A good example of wrong stress in diagnosis is the so-called aversion to fatty food. We made a particular point of this in histories, and practically none of our patients had themselves noted that fats upset them; without exception they were avoiding fats, when we saw them, because they had been told to do so by their doctor, but were not noticeably better for the deprivation. Contrast this with the peptic ulcer patient, who without any expert advice rapidly learns what he can and cannot eat—and fried food is usually high on his danger list.

Jaundice occurred in 18.1% of the cases reviewed by Adams and Stranahan. These investigators are of the opinion that jaundice indicates common-duct stones in only 50% of cases; in the remainder they postulate that jaundice, when present, is due to an associated hepatitis or cholangitis.

Analysis of 100 Cases of Cholelithiasis

Our data have been collected from the records and statements of 100 patients with cholelithiasis treated at this hospital between April, 1946, and April, 1951; all were interviewed personally.

Age and Sex Incidence.—It is recognized that gall-stones may occur at any age, even in infancy. Potter (1928) reported a case in a child aged 4½ years, while Dessau (1943), reviewing the higher age groups, stated that after the age of 40 years the incidence rises rapidly. In our series the peak incidence occurred between the ages of 41 and 60 (see Chart), with a secondary peak between the ages of 61 and 70 years. These findings confirm earlier work by Dessau (1943) and Robertson (1945). Marshall and Phillips (1948) noted the close parallelism between the



Age incidence in 100 cases of cholelithiasis.

age incidence of acute cholecystitis and that of cholelithiasis, and stated that 38% of their cases were 60 or over. In our series 27% were over 60 (see Chart). With regard to sex incidence, there is general agreement that this disease shows a marked predilection for the female; our figure (Table I)

TABLE I.—*Sex Incidence and Ratio of Female and Male Cases*

No. of Cases	Female	Male	Ratio F: M
100	83	17	4·8:1

of nearly 5:1 in favour of the female is supported by Weiss, though it is higher than the figures of Robertson (2:1), Adams and Stranahan (3:1), and Marshall and Phillips (2:1). Over 80% of the female patients in our series gave a past history of one or more pregnancies, the average number of children in the family being three.

Familial Incidence and Diathesis.—Weiss postulates a hereditary predisposition to cholelithiasis. We are impressed by the fact that 20.8% of our cases gave a positive family history of the disease (Table II). Furthermore, in parental

TABLE II.—*Analysis of Familial Incidence, Weight, and Parity in 100 Cases of Cholelithiasis*

No. of Cases	Familial Incidence	Average Weight		Parous Females
		Female	Male	
100	20·8%	151 lb. (68·5 kg.)	142 lb. (64·4 kg.)	80·7%

disease the same female predilection was noticeable: in no case was there an instance of gall-bladder disease occurring in the father or grandfather of the patients concerned. Marshall (1950) states that there is an increased incidence of gall-stones in the obese. The average weight of the females in our series exceeded the average weight of the males; in health it is generally accepted that the male on the average weighs more than the female. It would thus seem that the male gall-stone patient tends to be thin or of average weight, contrary to the female. The weight of 65% of our female cases was 140 lb. (63.5 kg.) or more.

Symptomatology.—We present our data in Table III; we have compared our findings with those published by Adams and Stranahan (1947). Although the present series is much

TABLE III.—*Analysis of Symptomatology of Present Series Compared with Lahey Clinic Findings*

Series	No. of Cases	Major Colic	Minor Colic	Nausea or Vomiting	Gall-Bladder Dyspepsia	Jaundice	Symptomless	Nocturnal Attacks
Present	100	46	50	68	56	24	4	38
Lahey Clinic* ..	1,104	93·2%		64·9%		18%	2·3%	—

* Adams and Stranahan (1947).

smaller than that of the Lahey Clinic investigators, the results are essentially similar. Table III shows that pain was the predominant symptom, occurring as major colic in 46% of the cases and as minor colic in 50%. Nausea and vomiting occurred in 68% and gall-bladder dyspepsia in 56%. Jaundice was noted in 24%, and in 4% the stones were apparently silent. The Lahey Clinic series does not mention the frequency of nocturnal pain, though we were impressed with the fact that many of our patients had pain only at night, and only on rare occasions during the day. We cannot suggest any explanation for this.

Discussion

This survey was undertaken because we were dissatisfied with our ability to diagnose cholelithiasis. We were surprised to find how little had been published in England in the last two decades, considering that the disease is so common. The writings and investigations which have been undertaken mostly derive from America. We have been able to confirm earlier observations on age and sex incidence, and have found the same relationships between pregnancy, obesity, and familial predisposition noted by other observers: admittedly our figures are small. We have drawn attention to certain similarities in the natural history of gall-stones and rheumatoid arthritis, and have offered the suggestion that deranged steroid metabolism may play as important a part in gall-stone formation as it has been shown to do in rheumatoid arthritis.

Our concern, however, was primarily with symptoms, and we have tried, as it were, to build up for ourselves a clinical picture anew, and clear our minds of preconceived notions. We feel satisfied that too much importance is often attached to "windy indigestion" and gall-bladder dyspepsia, so that diagnosis suffers, and have drawn attention to the value of a more careful assessment of the type of pain described by the patient. We have introduced the term "minor colic" to emphasize this; and by that term we mean a right subcostal pain of considerable severity, occurring with sufficient frequency to be of diagnostic value. There will still, however, be the residue of cases in which the discovery of gall-stones will come as a surprise, and it is concerning this group of patients that we must be most careful to ask ourselves whether the demonstrated stones are indeed causing the symptoms. It is generally accepted, of course, that the discovery of gall-stones is an indication for their removal in the majority of cases, and we agree with this, but it should not blind us to the possibility that some other abdominal disorder altogether may be accounting for the presenting symptoms. Clinical enthusiasm may so easily make us forget that the only concern of the patient is to be freed of his symptoms; and he is entitled to expect this if he undergoes the ordeal of an operation.

Summary

The aetiology of cholelithiasis is reviewed; the possibility of an underlying disturbance of steroid metabolism is postulated as the predisposing factor.

Symptomatology is discussed, and emphasis in diagnosis placed on pain rather than flatulent dyspepsia.

One hundred proved cases of cholelithiasis are analysed from the clinical aspect.

Our thanks are due to the consultant physicians and surgeons at the General Hospital, Birkenhead, who have kindly allowed us access to their cases.

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During 1951 the Ministry of Health lent their three portable exhibition sets on food and drink infections to 29 authorities for showing at clean food, health, and civic weeks throughout the country. The sets have now been entirely renovated and can again be borrowed by local authorities. Each shows by means of pictures and small models how food can become infected by those who handle it, and how a few simple precautions can guard against food-poisoning. A set consists of three units, each occupying approximately 24 sq. ft. There is no charge, but a local authority is expected to pay for transport and be responsible for erection, dismantling, and repacking of the exhibits. This can be done by unskilled labour under proper supervision.

PULMONARY TUBERCULOSIS AND PREGNANCY

BY

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Before the last two decades it was widely believed that pregnancy had a uniformly unfavourable effect on the course of pulmonary tuberculosis. This view has been contradicted in recent years by many authors, notably Cohen (1946), who gives an extensive review of the literature, and Stewart and Simmonds (1947). Brooks (1940) remarks that "scarcely any accurate scientific data exist by which the hypothetical effect of pregnancy on pulmonary tuberculosis may be evaluated." This is probably less true to-day than it was ten years ago; and certainly such evidence as has been accumulated supports the view that pregnancy in general has no dramatic effect on the course of the disease.

Present Investigation

An inquiry has been conducted into the experience of a selected group of women with pulmonary tuberculosis with regard to the incidence of pregnancies. The course of the disease was followed in those women who became pregnant; they were divided into two groups—those allowed to proceed to term and those whose pregnancies were terminated surgically.

Material.—The case histories of all sputum-positive tuberculous women of child-bearing age (17 to 45 years) who were admitted to the Brompton Hospital during 1945 and 1946 were investigated. Of the total of 508 women listed the case notes of 22 were not available and a further 24 have been lost sight of. The remaining 462 were followed up to December, 1950, and those who were found to have had pregnancies were selected for further study.

Mortality.—By the end of 1950, after an average period of observation of five years, 108 patients (23.4%) were dead. This low figure may be accounted for largely by the tendency to select for admission cases suitable for treatment.

Pregnancies.—There were 87 pregnancies in 65 patients. Of these pregnancies 24 were terminated and 63 proceeded to term. Two completed pregnancies occurred in each of seven patients and one only in each of 46. Two patients had one pregnancy completed and one terminated, and one had one completed and two terminated. Sixteen patients had one therapeutic abortion only and two had two abortions.

Fertility.—"Fertility" is used here to describe the occurrence of live births. The number of live births per 1,000 observation years in each five-year age group of this series of patients has been compared with the equivalent number taken from the Registrar-General's returns for the general population (Table I). In this way an indication of the fertility of women with pulmonary tuberculosis has been obtained. As might be expected, they have a very low birth rate compared with women of the same age groups in the general population: in the largest age groups it was approximately one-quarter of that for the general population. As only 24 pregnancies out of a total of 87 were artificially terminated, it is clear that the pregnancy rate also is very low. This comparison is based on the assumption that the proportion of married women to single is the same in this group as in the same age groups in the general population, whereas in this group the proportion may well have been lower. (The exact proportion is not known, as the date of marriage was not always available.) Further possible reasons for the low fertility rate are prolonged stay in hospital and contraceptive advice.

TABLE I.—*Live Births per 1,000 Observation Years in This Series, Compared with the General Population (Five-year Age Groups)*

Age Group (Years)	Patients	Observation Years†	Live Births	Live Births per 1,000 Obs. Years	
				This Series	General Population
15–19	56*	280	1	3·6	19·3
20–24	152	760	25	32·9	146·0
25–29	150	750	27	36·0	169·7
30–34	87	435	6	13·8	117·6
35–39	15	75	4	53·3	65·6
40–44	2	10	0	0	19·4
Total..	462		63		

* Only patients aged 17–19 were included.
† Number of patients multiplied by five. The average period of observation for each age group was approximately five years, as all cases were admitted during 1945 and 1946 and observed until December, 1950. This approximation probably has only a very slight effect on the results.

Tuberculosis First Diagnosed Shortly After a Pregnancy.—The history of tuberculosis becoming manifest within a few weeks of delivery is sometimes held to be evidence that pregnancy activates the disease. In the present series (486 cases—that is, those whose case notes were investigated, including those lost sight of) the diagnosis is recorded as having been made within three months of delivery in 13 only; these 13 pregnancies, of course, fall outside the period of observation and are not included in the main series. It is seen from Table II that the incidence of this particular history in the present series is not greater than would be accounted for by chance. The percentage of women in each age group of the general population who can be expected to be within three months of delivery of a child at any given time has been calculated from data given in the Registrar-General's returns. It was found that these figures do not differ significantly from the percentage of patients in each age group of the present series who were diagnosed within three months of delivery.

TABLE II.—*Percentage of Patients Diagnosed Within Three Months of Delivery, Compared with Percentage of Women in the General Population Expected to be Within Three Months of Delivery at any Given Time*

Age Group (Years)	Total No. of Patients	No. Diagnosed Less than Three Months after Delivery	Percentage Diagnosed Less than Three Months after Delivery	Percentage of Women in General Population who Expect to be Within Three Months of Delivery
15–19	56*	1	1·8	0·5
20–24	152	5	3·3	3·9
25–29	150	3	2·0	4·3
30–34	87	3	3·4	3·2
Total..	445	12		

* Only patients aged 17–19 are included.
Age groups 35–39 and 40–44 years each contained fewer than 50 patients, and are therefore not included. One patient in the 35–39 age group was diagnosed less than three months after delivery.

Analysis of Completed Pregnancies

In assessing the effect of pregnancy on pulmonary tuberculosis the nine pregnancies which occurred in 1950 have been omitted from the analysis. The remaining 54 pregnancies occurred in 47 patients, seven of whom had two pregnancies each. These 47 patients have been divided into two groups: "Active," with evidence of activity at the time of diagnosis of pregnancy (13 patients); and "non-active," without evidence of activity at the time of diagnosis of pregnancy (34 patients). The results of the follow-up of each of these two groups have been compared with those of the similar groups whose pregnancies were terminated surgically. The results, summarized in Tables III and IV, show that they are strikingly similar.

Active.—In these 13 patients the evidences of activity were persistent cavitation in seven, radiological spread occurring

TABLE III.—*Active Group. Comparison Between 15 Completed Pregnancies in 13 Patients and 6 Terminated Pregnancies in Six Patients, Showing Periods of Observation, and Number who Later Deteriorated, Improved, or were Unchanged*

	Completed Pregnancies					Terminated Pregnancies				
	Period of Observation after Delivery				Total	Period of Observation after Termination				Total
	1–2 yrs.	2–3 yrs.	3–4 yrs.	4–5 yrs.		1–2 yrs.	2–3 yrs.	3–4 yrs.	4–5 yrs.	
Total No. of pregnancies ..	5	4	5	1	15 (13 patients)	3	2	0	1	6
No. followed by deterioration ..	4	1	2	1	8 (7 ,,)	3	1	0	1	5
No. unchanged	1	2	2	0	5 (4 ,,)	0	1	0	0	1
No. followed by improvement ..	0	1	1	0	2 (2 ,,)	0	0	0	0	0

Of the two patients having two completed pregnancies, one showed no change 26 months after her first, and 13 months after her second; the other was following a very gradually downhill course 41 months after her first pregnancy and 28 months after her second.

TABLE IV.—*Non-active Group. Comparison Between 39 Completed Pregnancies in 34 Patients, with 14 Terminated Pregnancies in 12 Patients, Showing Periods of Observation, and Number who Later Deteriorated, Improved, or were Unchanged*

	Completed Pregnancies					Terminated Pregnancies				
	Period of Observation after Delivery				Total	Period of Observation after Termination				Total
	1–2 yrs.	2–3 yrs.	3–4 yrs.	4–5 yrs.		1–2 yrs.	2–3 yrs.	3–4 yrs.	4–5 yrs.	
Total No. of pregnancies ..	19	10	5	5	39 (34 patients)	4	5	3	2	14 (12 patients)
No. followed by deterioration ..	3	1	1	2	7 (7 ,,)	2	1	0	0	3 (3 ,,)
No. unchanged	13	7	4	2	26 (21 ,,)	1	3	2	2	8 (6 ,,)
No. followed by improvement ..	3	2	0	1	6 (6 ,,)	1	1	1	0	3 (3 ,,)

less than three months before pregnancy in four, and pleural effusion (tubercle-positive) in two. Seven patients deteriorated, four have shown no change, and two have shown radiological improvement (Table III). Of the seven who deteriorated, two did so during pregnancy, two less than three months after delivery, one eight months, one nine months, and one four years after delivery. Two of these died—one after 19 months and one after three years. Of the seven patients who, despite treatment, showed persistent cavitation during pregnancy, six deteriorated subsequently.

Non-active.—This group of 34 patients includes all those without cavitation in whom no radiological spread had been observed in the three months before conception. The term non-active is therefore clearly not equivalent to quiescent as ordinarily defined. Five of these patients each had two pregnancies. In seven patients pregnancy was followed by deterioration, 21 have shown no change, and six have shown radiological improvement. Of the seven who deteriorated, one did so during pregnancy, one six weeks after delivery, two nine months after, one a year after, one two and a half years after, and one three and a half years after. Four of these seven had two pregnancies, the deterioration in each case occurring after the second. The fifth patient, who had two pregnancies, remained unchanged during the 15 months for which she was observed after her second child.

Patients in Whom Pregnancy was Terminated

Three patients had a completed pregnancy as well as therapeutic abortion. Of these, one had a termination three years after a completed pregnancy, although her chest condition was apparently stable; two had pregnancies terminated shortly after tuberculosis was diagnosed, but, after intervals of two and three years, respectively, had a completed pregnancy without any adverse effect on the tuberculosis.

Apart from these, 20 pregnancies were terminated in 18 women, two of whom had two terminations. These 18 patients were divided into active and non-active groups, using the same criteria as for the completed pregnancies. Six were active cases, of whom five had persistent cavitation and one had a spread of infiltration less than three months before termination. Of these, five subsequently deteriorated—two immediately, one after one year, one after 18 months, and one after four years; and one remained unchanged. Of the five patients with persistent cavitation, four subsequently deteriorated. Twelve were non-active—in three the abortion was followed by deterioration after two months, 15 months, and 30 months; in six by no change; and in three by improvement. Both the patients having two terminations came into this group, and have subsequently remained well.

Discussion

As the definition of activity and quiescence is at best a very arbitrary matter, it was decided to call "active" only those cases with definite evidence of activity at the time of diagnosis of pregnancy. All cases were sputum-positive, and therefore active, on admission; it follows that a proportion of the non-active patients were not yet quiescent, according to the usual definition, when pregnancy was diagnosed. By defining activity and non-activity in this way a bias has been introduced, the effect of which is to magnify to some extent the possible effects of pregnancy on the course of the disease.

The series is too small for any definite conclusion to be drawn with regard to the question of whether a particular patient with pulmonary tuberculosis should or should not have a pregnancy terminated; but the proportions subsequently deteriorated, unchanged, or improved in each group—that is, allowed to continue and terminated—are strikingly similar. If the two groups are comparable in other respects, as they appear to be, then from the evidence presented in this series there is no indication for therapeutic abortion, as the outcome seems to be similar whether the pregnancy is terminated or not.

There is likewise no evidence that pregnancy, whether terminated or allowed to continue, had any definite effect on the course of the disease in this series of patients. The overall survival rate of sputum-positive cases of pulmonary tuberculosis five years after diagnosis is given by Tattersall (1947) as 32% and by Berg (1941) as 33%. Berg gives a slightly lower survival rate for women of the child-bearing age groups. The very serious prognosis of sputum-positive tuberculosis, in spite of modern methods of treatment, should be kept in mind when considering the course of the disease in women who have also had pregnancies. Stewart and Simmonds (1947) found no significant difference between their pregnant and non-pregnant—that is, control—groups of tuberculous patients with regard to the course of the disease over a follow-up period of 12 to 15 months.

Summary

A group of 462 women with pulmonary tuberculosis, who were observed for an average period of five years,

have been studied, with particular regard to the incidence of pregnancy and its effect on the tuberculosis.

There were 54 completed pregnancies in 47 patients, who were followed up for at least one year after delivery; 20 pregnancies in a further 18 patients were artificially terminated.

The patients with completed and interrupted pregnancies were each divided into two groups—those with active and those with non-active disease. In each of these groups the results in patients with completed and those with interrupted pregnancies did not differ appreciably at the end of the follow-up period.

Of patients with persistently patent cavities in spite of treatment, seven completed their pregnancies, and of these, six later deteriorated. Of five whose pregnancies were terminated four later deteriorated.

As expected, the birth rate among these patients was very low, being of the order of one-quarter of that for women of the same age groups in the general population.

The initial diagnosis of tuberculosis less than three months after an antecedent pregnancy was not made with greater frequency than could be ascribed to chance.

The findings support the view that pregnancy has no very dramatic effect on the course of pulmonary tuberculosis.

I wish to record my thanks to Dr. J. G. Scadding for his help and encouragement in writing this paper; to Mr. P. Armitage, of the Statistical Research Unit, Medical Research Council, for providing the figures from the Registrar-General's returns and for much helpful criticism; to the medical committee and individual physicians at the Brompton Hospital for access to the case records and for permission to publish; and to the many chest physicians who have so fully answered my postal inquiries.

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Irish medical students now approaching the end of their training are hoping that British hospitals will be able to offer them jobs next year, otherwise they may be delayed for some time before they are able to set up in practice on their own. New Irish legislation, expected to come into force next January 1, will require all newly qualified doctors leaving medical school to work in a hospital for a year before their names are entered on the *Irish Medical Register*. This is part of the arrangement with Britain about the new intern year. But between 260 and 270 students are expected to qualify in Dublin next year, and there will be only 200 jobs available for them in Irish hospitals. They understand there will be about 100 jobs available for them in British hospitals. If these jobs do not materialize, however, there is likely to be a waiting-list of medical students who have completed their training but have not qualified for practice. There is an inducement to them to work in Britain. In Irish hospitals the young doctors will be paid £150 for their year's work, plus their keep. In Britain the pay is £375, from which £100 is deducted for keep. Irish hospitals are wondering where they are to get the money to pay these salaries. "The increase in cost cannot be less than £50,000 a year," says Dr. R. A. Stoney, president of the Irish Medical Registration Council, in a paper published in the current *Irish Journal of Medical Science*. "So far there has been no authoritative statement as to where this money is to come from."

VALUE OF PNEUMOENCEPHALOGRAPHY IN DIAGNOSIS OF FITS

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The occurrence of fits in a young and otherwise healthy adult who has no abnormality on clinical examination is fairly frequent in neurological practice among the armed Forces. Once there is convincing clinical evidence that they are genuine epileptic attacks, the further problem arises whether they are idiopathic (constitutional) or symptomatic of some organic lesion of the brain, such as a neoplasm, cicatrix, angiomatous malformation, or the like. Help in deciding this is given by the family and personal history. Useful evidence may also be obtained from examination of the cerebrospinal fluid (C.S.F.), *x*-ray films of the skull, and electroencephalograms. None of these procedures causes much clinical upset, and, provided facilities are available, they are not time-consuming. They may, however, give equivocal results; if they are negative the clinical setting of the epilepsy may still leave the suspicion of a possible progressive intracranial lesion as a causative factor. In that case it is usual to consider the advisability of doing pneumoencephalograms to see whether there is displacement or distortion of the ventricular system or whether there are abnormalities in the disposition of cortical air. This procedure does temporarily upset patients, and it carries a slight but definite risk. It is pertinent, therefore, to ask how much useful diagnostic information is likely to accrue in the clinical setting mentioned above.

The possibility of a cerebral neoplasm presenting as epilepsy in a young adult cannot be ignored. Thus, Penfield and Erickson (1941) tabulated the presumptive causes of epilepsy appearing at different ages, and for the age group 20 to 35 years they put first trauma and then neoplasm. (It is worth noting that neurosyphilis, still often invoked in many standard textbooks, is not considered important, an opinion with which most neurologists practising in this country would agree.) Discussing this table, they wrote: "In young manhood and in middle age the onset of epilepsy without obvious traumatic cause should always suggest an expanding lesion as the most likely cause." They also declared: "In general, all patients whose seizures have come on late in life should come in for study and usually pneumography." Notkin (1931), studying chronic epileptics with mental deterioration, found that only 8 out of 17 cases had normal pneumoencephalograms. Dickerson (1941), on the other hand, found only 7 abnormal encephalograms in 313 studies on epileptics, but he did not state the type of case he was studying. Merritt and Brenner (1944) reported three patients who had pneumoencephalograms done 7, 20, and 30 months respectively after their first fit. All the encephalograms were normal, and no patient had any abnormal physical

signs, yet all three were eventually proved to have a cerebral tumour. A study of pneumoencephalogram findings in cases of patients who present with epilepsy of recent onset and with no abnormal signs in the central nervous system does not seem to have been made. If abnormalities can be found at this stage the procedure should clearly be widely used, even if normal air pictures cannot be taken to exclude neoplasm. The present study was therefore undertaken to provide information on this point.

Material

During the six years 1945–50, 64 patients were subjected to pneumoencephalography at a military hospital for head injuries because of the development of fits. In eight of these the records were unsatisfactory because of insufficient air or because the air had not entered the ventricles. There remained 56 cases which were taken for review here. All but three were males. In every case the evidence that the fits were epileptic in character was satisfactory and none had begun earlier than the age of 18. Only four had convincing clinical abnormalities in the central nervous system. Cases of blunt head injury such as might be sustained by any civilian patient are included, though none of these were recent and none had residual neurological signs at the time of examination. No penetrating brain wounds are included. The material is selected, since cases with changes initially suggesting localized cerebral disease were excluded, but it represents the not uncommon neurological problem of "fits for investigation."

The ages of the patients at the onset of the attacks are given in Table I. The length of time which had elapsed between the occurrence of the first attack and the performance of pneumoencephalography is shown in Table II. The frequency of the attacks is given in Table III.

TABLE I.—*Ages at Onset of Attack*

18–20 years	11 cases	31–35 years	13 cases
21–25 ,,	15 ,,	36–40 ,,	11 ,,
26–30 ,,	3 ,,	Over 40 ,,	3 ,,

TABLE II.—*Time of Pneumoencephalography Since Onset of First Fit*

One month	7 cases	Three years	5 cases
Three months	10 ,,	Five ,,	6 ,,
Six ,,	11 ,,	Over five years	5 ,,
One year	12 ,,		

TABLE III.—*Frequency of Attacks*

One attack only	5 cases	Once in six months or more	16 cases
Once a week or more	12 ,,	Less than once in six months	3 ,,
Once a month or more	18 ,,	Unknown	2 ,,

There were 39 examples of grand mal, 15 of Jacksonian attacks, 3 of petit mal, and 2 of akinetic attacks. Three patients had two sorts of attacks: 2 had grand mal with petit mal and 1 had Jacksonian attacks with petit mal.

There was no family history of epilepsy in 49 cases, 5 had a positive history, and in 2 there was no information. The previous medical history contained nothing of significance in 40 cases; 12 had had head injuries, but in all except 2 of these the post-traumatic amnesia had been less than 24 hours; one was a professional boxer; one had a history of cerebral thrombophlebitis, one of neurosyphilis which was sero-negative at the time of examination, and one of meningococcal meningitis. There were no abnormal signs in 52 cases, 3 had slight motor changes such as increased reflexes or slight loss of power, and 1 had a hemianaesthesia and hemianopia in addition to slight spastic hemiparesis.

Of the 56 cases, 42 had electroencephalograms done. Twenty of these had normal records, 13 had a bilateral generalized dysrhythmia, in 5 the dysrhythmia was more marked on one side than the other, and 4 showed a definite focal disturbance.

In 41 cases of the series the result of C.S.F. examination was normal. In 2 the protein was over 50 mg. and in 4 between 45 and 50 mg. In 9 the results were not available. Only one of the cases with raised protein showed abnormality of air pictures.

Technique

Pneumoencephalography was done by the lumbar route with the patient in the sitting position in all cases. Thirty-five to 50 ml. of C.S.F. was removed by repeated aspiration, and after each removal air was injected. After a check film with the patient still sitting up, standard views in the brow-up and brow-down positions were taken. Views for third and fourth ventricles, and in most cases laterals and postero-anterior views with the patient erect to outline the roof on the lateral ventricles, were also done.

In 51 cases the air pictures were normal, 3 were abnormal, and in 2 there was a doubtful abnormality. In these two there was a difference of opinion between radiologists and neurologists. In each case the former considered the pictures within the range of normal, whereas the latter thought they showed a recognizable local abnormality. Details of these last five cases are given because they illustrate the diagnostic problems.

Case Reports

Case 1.—A young man aged 20 had sustained a head injury six years previously, with fracture of the right frontal bone and a post-traumatic amnesia of one week. He had made an uneventful recovery. Three months before admission he had begun with grand mal attacks, of which he had four in all. Physical examination was negative, and there was no family history of epilepsy. C.S.F. was normal. Straight *x*-ray films of the skull also showed no abnormality. The electroencephalogram revealed some slowing in the right frontal region. The pneumoencephalogram showed slight indentation in the roof of the anterior horn of the right ventricle. In view of the normal C.S.F. and the history of head injury the most probable diagnosis in this case was considered to be traumatic epilepsy.

Case 2.—A man aged 33 began with grand mal attacks one year before he was seen. These had continued with a frequency of one a month. There was no previous relevant medical history, and abnormal signs were absent. The family was free from epilepsy. *X*-ray films of the skull showed an island of denser bone in the right frontal region, but no other abnormality. C.S.F. was normal and the blood W.R. negative. A pneumoencephalogram showed some degree of dilatation of the lateral ventricles which was quite symmetrical.

Case 3.—A man aged 21 began six months previous to admission with grand mal attacks, of which he had two. There was no previous medical history or any relevant family history. Examination, however, showed mild weakness and slight smallness of the right side of the body, with sensory loss and a right homonymous hemianopia. The electroencephalogram showed a persistent depression of the dominant frequency throughout the left hemisphere. C.S.F. was normal. Air pictures revealed a large porencephalic cyst in the left parieto-occipital region communicating freely with the ventricle.

Case 4.—A previously healthy man aged 26 suddenly had a right-sided sensory seizure one evening. This occurred some four weeks before admission to the head injuries hospital. He had a history of a blow on the face some weeks before the fit, but had had no loss of consciousness at this time. Within three weeks of his first fit he had several others, and after the third had some right-sided facial weakness with minimal weakness of the right hand also, and a doubtful right extensor plantar response. C.S.F. showed 50 mg. of protein, but no other abnormality. These signs had persisted for a month when he had his pneumoencephalogram done. This did not show any displacement

or distortion of the ventricular system, which was well filled, but the left temporal horn seemed flatter than the right. The significance of this was disputed, but the finding, combined with his slight right-sided signs, led to ventriculography, in which the change in the left temporal horn was again seen. Brain biopsy was done in the temporal region, but only normal brain was recognized. After this his signs slowly receded. Some months later he had had no further fits, but still had a slight facial weakness. The most probable diagnosis clinically was thought to be an infiltrating glioma. No further follow-up was possible.

Case 5.—During a period of 24 hours a man aged 26 had a series of attacks of unheralded loss of consciousness, with convulsions beginning in the left arm and rapidly becoming generalized. Before the fits he had noticed no disability; after them he was aware of some fumbling in the use of the left hand, and examination showed slight but undoubted weakness of the left limbs. C.S.F. and skull examinations were normal. Pneumoencephalograms were done within a month of the seizures. The right lateral ventricle was slightly larger than the left, and there was a depression in the roof of the anterior part. The significance of these findings was disputed. Nevertheless, as his physical signs steadily increased and his state of responsiveness deteriorated, ventriculograms followed by craniotomy were done about three weeks later. The ventriculograms showed a slight filling defect of the right anterior horn, and at operation an infiltrating glioma of the corpus callosum involving both frontal poles, right more than left, was revealed.

Discussion

The interpretation of air pictures with minor degrees of abnormality is often difficult, and it is not uncommon to review pictures in the light of subsequent clinical events and see abnormalities which were missed at the time. In all the cases recorded here an opinion was given independently both by neurologists and by radiologists.

In this series of 56 young adults presenting with epilepsy, only three showed clearly abnormal air pictures. In two further cases there was disputed abnormality. Moreover, a history of severe head injury some years before in one of these five, and the presence of unequivocal abnormal neurological signs in three others, suggested that their epilepsy was symptomatic and that abnormality of air pictures might be found. The main bulk of the cases, however, had no such clinical indication of the possible source of their attacks. None had had attacks until adult life, and in 49 of them there was no family history of epilepsy or related phenomena. They were therefore cases in which, according to Penfield and Erickson (1941) intracranial neoplasm was a likely cause of their attacks. Nevertheless, of the cases in which nothing apart from seizures suggested underlying brain disease, in only one was the air picture abnormal. The type of fit also did not seem to help in indicating when abnormality might be found. Jacksonian attacks suggesting a possible focal lesion were found in 15, but of these, 13 had normal air pictures, and in only 2 was there doubtful abnormality; while each of the 3 in which there were definite abnormalities had generalized grand mal attacks with no focal onset.

Unfortunately these patients were invalided out of the Service and their further history is not available. It is possible that some of them would subsequently have developed clear evidence of gross intracranial disease, as in the cases followed by Merritt and Brenner (1944). Nevertheless, it seems justifiable to conclude that when epilepsy presents in young and otherwise healthy adults with no clinical signs of involvement of the central nervous system, intracranial air studies are not of much diagnostic value. It is important to emphasize that we are speaking of young and healthy adults who showed no abnormality on a searching neurological examination, and to add that there will be some patients within this group for whom the results of other investigations—in particular, abnormalities of C.S.F. protein, or localized or focal electroencephalographic changes—will still demand air pictures. In general, however, even if we accept the view that intracranial neoplasm is a likely cause for the attacks, the results in this small series suggest that it would be wiser to keep such patients under regular neurological observation and withhold a procedure which carries a slight but definite risk until changes in the clinical picture suggest that it will yield useful information.

It is possible that cerebral angiography may in the future provide a more useful diagnostic guide in this problem—particularly where a focal onset to attacks provides information about which side should be injected. As yet, further experience of its use in the type of case here discussed is required.

Summary

Fifty-six patients who had epilepsy in early adult life were subjected to pneumoencephalography. Four had had abnormal physical signs; three of these had definitely abnormal air pictures, and the fourth a doubtful abnormality. Of the 52 cases with no abnormality on clinical examination, 51 had normal air pictures.

It is suggested that the diagnostic value of pneumoencephalography in young adults with epilepsy as their only abnormality is not great, and that it is better to keep these patients under neurological observation until the emergence of clinical signs indicates the need for air studies.

Permission to publish was given to one of us (J. M.) by Brigadier W. R. D. Hamilton, A.M.S., consultant physician to the War Office. Our thanks are due to medical officers at the military hospital for head injuries, whose detailed clinical notes were invaluable in those cases not seen personally by us; to the radiologists who reported on films; and to Dr. W. Ritchie Russell and Mr. Joe Pennybacker for comments and criticisms.

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The means of suicide are changing. The once popular method of poisoning with phosphorus has given way to the use of narcotics. In *Casopis Lekaru Ceskych*, E. Vencovsky and A. Reisich report the first suicidal attempt in Czechoslovakia with "antabuse" (tetraethylthiuramdisulphide) and alcohol in a chronic alcoholic who was being treated at the time with antabuse. The amount of alcohol leading to fatal intoxication varies with the concentration of alcohol, the tolerance of the individual, and the presence of intercurrent or latent diseases. A blood level of approximately 0.6% is generally accepted as fatal. Antabuse is practically a non-toxic substance, and its effect is based on the inhibitory action of complete oxidation of the ingested alcohol. The oxidation is arrested at an intermediate state, when acetylaldehyde is produced. The resulting acetaldehydaemia leads to a temporary intoxication with very unpleasant signs and symptoms that deter the individual from further alcohol consumption. As the antialcoholic action develops only after some days, treatment has to be administered two or three days weekly. Fatal accidents have been seen only in a few cases where contraindications have been disregarded (two cases in Czechoslovakia and seven elsewhere). The intensity of action depends upon the amount of alcohol consumed at one time. The patient under observation, living under great emotional stress during antabuse treatment, attempted suicide by drinking one pint (0.57 l.) of brandy.

ISOLATED NEURITIS OF THE ANTERIOR INTEROSSEOUS NERVE

BY

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Lesions of the anterior interosseous branch of the median nerve have been recorded so infrequently that this description of two cases of isolated neuritis of the nerve seems justifiable. The deep position of the nerve protects it from trauma, and when damage does occur it is to be expected that the median nerve—and perhaps the long flexor tendons—will also be affected. Puncture wounds of the forearm are the most likely cause of injury to the nerve. It is probable that examples of neuritis of the nerve occur more commonly than is generally recognized, for the resulting disability is not severe, accommodation occurring quickly in most patients, while recovery follows in many.

Case 1

A man aged 52 noticed suddenly on February 7, 1949, that he was unable to pick up small objects with his right hand. He found that the thumb and radial two fingers were weak. He had no paraesthesiae or numbness and no pain in the arm or hand, though subsequently he noticed an aching pain along the medial border of his right forearm when grasping objects. After three or four days there was some improvement of the fingers, but not of the thumb. His general health had been good and he made no other complaints. There was nothing relevant in his previous medical history.

When seen on February 21, 1949, there was complete paralysis of the right flexor pollicis longus, moderate weakness of the head of the flexor digitorum profundus to the index finger (M.R.C. scale, 3), and less marked weakness of the head to the middle finger (4−). The remainder of the flexor digitorum profundus, the flexor digitorum sublimis, and all the small muscles of the hand were normal. There was no sensory impairment, and in all other respects the nervous system was normal. The electrical reactions of the muscles of the right forearm showed complete reaction of degeneration in the flexor pollicis longus and the radial half of the flexor digitorum profundus. The reactions of the medial half of the flexor digitorum profundus, the pronator teres, and the flexor carpi radialis were normal. The blood Wassermann reaction was negative.

In January, 1950, the power of the long flexors of the index and middle fingers began to improve, and in March a feeble contraction of the flexor pollicis longus could be appreciated. By January, 1951, considerable recovery had occurred (flexor pollicis longus 3+; flexor digitorum profundus to index finger 4+, and to the middle finger 5).

Case 2

A man aged 28 awakened one morning in January, 1950, with pain along the outer aspect of the left forearm and a feeling of stiffness in the left thumb. He found that he was unable to bend the terminal joint of his thumb. The pain disappeared after two weeks. He continued at work as a glazier, but had difficulty in picking up small objects with his left hand. He denied any weakness of his index finger.

He was not seen until November, 1950, when examination revealed a complete paralysis of the left flexor pollicis longus. No other muscles were affected, and there was no sensory loss. The nervous system was otherwise normal. The left flexor pollicis longus showed complete reaction of degeneration. No other muscles were tested. The blood Wassermann reaction was negative.

The patient was treated with galvanism, and when seen in January, 1951, active flexion of the terminal joint of the left thumb was again possible (M.R.C. scale, 3). By April further improvement had occurred (4−).

Discussion

The anterior interosseous branch of the median nerve is given off a short distance below the elbow and runs distally on the volar aspect of the interosseous membrane, accompanied by the anterior interosseous artery. It lies between the flexor pollicis longus and the flexor digitorum profundus, overlapped by both, and passes deeply beneath the pronator quadratus, its terminal twigs supplying the wrist-joint. It innervates the flexor pollicis longus, the radial portion of the flexor digitorum profundus, and the pronator quadratus. It contains no fibres subserving superficial sensation.

In Case 1 the weakness was precisely in the distribution of the anterior interosseous nerve. The fact that the paralysis of the heads of the flexor digitorum profundus to the index and middle fingers was not absolute does not necessarily indicate that the nerve lesion was incomplete, for, as has been shown by Sunderland (1945), there is considerable individual variation regarding the proportions of this muscle supplied by the median and ulnar nerves. In some, the slip to the middle finger is entirely supplied by the ulnar nerve. No assessment of the function of the pronator quadratus was made, for it belies its name in being a very feeble pronator of the forearm. Its main action is to prevent separation of the radius and ulna when pressure is exerted on the carpus, a function not readily susceptible of clinical evaluation. Unfortunately the electrical reactions of this muscle were not investigated.

In Case 2 only the flexor pollicis longus was affected. When seen nearly a year after the onset of the paralysis, the patient denied any other weakness, and there is no reason to doubt his statement. Any pathological process capable of picking out the anterior interosseous nerve might as easily select a subdivision of it, and in the great majority of individuals the flexor pollicis longus is innervated by a single branch of this nerve (Sunderland, 1945).

In view of the sudden onset and the delayed partial recovery of these two cases, they would appear to be examples of an interstitial neuritis analogous to the series of cases of acute brachial neuritis described by Spillane (1943). The onset and course of the condition are unlike those of acute anterior poliomyelitis.

References to lesions of the anterior interosseous nerve in the literature are remarkably scanty. Involvement by penetrating wounds of the upper forearm has been reported by Borchardt and Wjasmenski (1917). These authors, together with Ranschburg (1917), suggest that in some cases showing isolated weakness of the long flexors of the thumb and index finger the lesion may affect the entire median nerve, the other muscles normally innervated by the median nerve receiving an aberrant supply from either the ulnar or musculo-cutaneous nerve. This view is repeated by Kinnier Wilson (1940). It is possible that this is the explanation of an occasional case, but in most—including those described above—there is no doubt that the lesion is restricted to the anterior interosseous nerve.

In a review of 136 cases of acute brachial neuritis (neuralgic amyotrophy) Parsonage and Turner (1948) described five patients in whom weakness of the long flexors of the thumb and index finger occurred in addition to shoulder-girdle weakness. In one the condition was bilateral, the thumb and index finger being affected on one side, the thumb alone on the other. A further case is described in which weakness of the left thumb and

index finger occurred as an isolated lesion. They conclude that such a "localized paralysis cannot anatomically be of peripheral-nerve or nerve-root distribution, and is only explicable by an anterior-horn-cell lesion." This conclusion is to be doubted in view of the fact that the weakness is in the distribution of the anterior interosseous nerve.

In both the cases described above it was approximately a year after the onset of the weakness that recovery began. In the absence of any recovery after a prolonged period, the question of a tendon transplant into the thumb would have to be considered. No decision should be made until at least 18 months after the onset. In the meantime the function of the denervated muscles should be maintained so far as possible by means of galvanism. Splinting is unnecessary.

Summary

Two cases of acute interstitial neuritis of the anterior interosseous nerve are described, one complete, the other affecting the branch to the flexor pollicis longus. Other examples of this condition found in the literature are reviewed.

We should like to express our thanks to Mr. H. L.-C. Wood for permission to report the second case.

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ON THE VERBAL USAGE OF THE CDE NOTATION FOR THE RH BLOOD GROUPS

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Since Fisher and Race published their theory of the triple allelomorphic nature of the Rh–Hr blood antigens and antibodies (see Race, 1944) there has been considerable discussion on the usefulness of their CDE notation as compared with the Wiener (1949) notations. One of the most frequent criticisms that have been made of the Fisher–Race notation is that it is difficult to use verbally. In spite of such an objection, we have found that the Fisher–Race system is complete, clear, and versatile enough to allow for the inclusion of new antigens and antibodies as they are discovered.

Method

In our laboratories there has evolved a verbal usage of the Fisher–Race notation that seems useful to the laboratory worker as well as to the clinician who is faced with an iso-immunization problem. In this system the genotype or "probable genotype" (Hill, 1947) is taken into account rather than the phenotype. Although our method is not offered as a panacea for this controversial subject, we feel that it has certain virtues, such as: (1) using the CDE notations verbally for both the antigens and the antibodies; (2) elimination of double symbols and double thinking in writing the CDE genotype and presenting it verbally; (3) consideration of the antigens present in an erythrocyte on a genetic basis; and (4) a presentation of usable information for clinical problems.

In Table I are presented some CDE genotypes, the Race short symbol for verbal usage, the Wiener (1949) terminology, and the method we have used in verbal presentations. In this latter system of verbal usage, only the CDE (Rh) antigens are given, with the cde (Hr) antigens left out but understood to be present. With this system the CDE antigens are regarded as closely linked genes inherited in groups of three. Consequently, the genotypes are given with consideration to both sides of the chromosomes—for example, CDe/CDe is called homozygous CD, whereas CDe/cde is called heterozygous CD, and Cde/Cde is called homozygous C, while Cde/cde is heterozygous C. Although the examples presented in Table I do not cover all of the CDE/cde (Rh–Hr) genotypes, a sufficient number are presented for an adequate demonstration of the system.

TABLE I

Genetic and Antigenic Constitution	Race Short Symbols	Wiener Terminology, 1949	Suggested Verbal Usage
cde/cde	rr	r^1r^1	Rh negative
CDe/CDe	R_1R_1	R^1R^1	Homozygous CD
CDe/cde	R_1r	R^1r	Heterozygous CD
CDe/cDE	R_1R_2	R^1R^2	CDDE or CD over DE
cDE/cDE	R_2R_2	R^2R^2	Homozygous DE
Cde/Cde	$R'R'$	$r'r'$	Homozygous C
Cde/cde	$R'r$	$r'r$	Heterozygous C
C^{v}de/cde	$R''r$	$r''r$	Heterozygous C^v
C^{v}de/C^{v}de	$R''R''$	$r''r''$	Homozygous C^v
cDe/cDe	R_0R_0	R^0R^0	Homozygous D
cDe/cde	R_0r	R^0r	Heterozygous D
cdE/cdE	$R''R''$	$r''r''$	Homozygous E
cdE/cde	$R''r$	$r''r$	Heterozygous E
CDe/cDe	R_1R_0	R^1R^0	CDD or CD over D
CDe/cdE	R_1R''	R^1r''	CD over E
CDe/Cde	R_1R'	R^1r'	CDC or CD over C
CDE/cde	R_2r	R^2r	Heterozygous CDE
CdE/CdE	R_yR_y	r^yr^y	Homozygous CE
C^{v}De/CDe	$R_1{}^vR_1$	R^3R^1	C^{v}DCD or C^{v}D over CD
C^{v}De/cDE	$R_1{}^vR_2$	R^3R^2	C^{v}DDE or C^{v}D over DE
CdE/C^{v}de	$R_yR''^v$	R^yr''	CEC^v or CE over C^v

It should be noted that the verbal usage of the CDE notation has already been successfully applied to the antisera for the Rh–Hr subgroups, using the same notation without special consideration for multiple specificity sera. Table II presents the already used antisera terminology as compared with that previously offered by Wiener.

TABLE II

Fisher–Race		Wiener	Fisher–Race		Wiener
Anti-C	..	Anti-rh′	Anti-D^u	..	Anti-Rh^u
Anti-D	..	Anti-Rh$_0$	Anti-E^u	..	Anti-??
Anti-E	..	Anti-rh″	Anti-CD	..	Anti-Rh$_1$
Anti-c	..	Anti-hr′	Anti-DE	..	Anti-Rh$_2$
Anti-d	..	Anti-Hr$_0$	Anti-C^{v}D	..	Anti-Rh$_0$‴
Anti-e	..	Anti-hr″	Anti-C^{v}C	..	Anti-rh‴rh′
Anti-C^v	..	Anti-rh‴	Anti-DD^u	..	Anti-Rh$_0$Rh^u

By comparing the Wiener notations of antigens (Table I) with antisera (Table II) one can readily see the changes in designations that are made between antigen and antibody. For example, the Rh antigen combinations are given without the h, such as r, r″, R′, while the corresponding antibody is designated as anti-rh′, anti-rh″, and anti-Rh$_1$. In addition to the deletion of the h, antigens have the subgroup designations above the r or R, and antibody subgroup designations are positioned below the rh or Rh.

In contradistinction to the Wiener usage, the Fisher–Race designations specify that the same letter used for the antigen be used for the antibody—that is, anti-c, anti-e, anti-CD, etc.

In view of the above verbal usage of the Fisher–Race nomenclature in what we feel is a successful manner, there is no longer that serious objection to the use of this system.

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RESPONSE OF THE MEGALOBLASTIC ANAEMIAS OF PREGNANCY TO ANIMAL PROTEIN FACTOR

PRELIMINARY REPORT

BY

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In previous communications we reported the response of the megaloblastic anaemias of pregnant and non-pregnant African women to injection of crystalline penicillin G (Foy *et al.*, 1951a, 1951b, 1951c). Continuing this work in the treatment of the megaloblastic anaemias of Africans, we are now able to report the response of the megaloblastic anaemias of pregnancy to A.P.F. (animal protein factor of Lederle, now known as "aurofax"). This substance is a fermentation product of *Streptomyces aureofaciens* and a by-product of the manufacture of "aureomycin." It contains at least four factors in each 250-mg. capsule—namely, A.P.F., 6.7 mg. of aureomycin, 1 μg. of vitamins B_{12a} and B_{12b}, and an "unknown factor."

Our patient took by mouth nine capsules a day. She thus received, in addition to the A.P.F. and unknown factor, 60 mg. of aureomycin and 9 μg. of vitamins B_{12a} and B_{12b} daily. On the seventh day of treatment there was a maximum reticulocyte response of 27%, followed by adequate red-cell and haemoglobin regeneration. No other treatment but A.P.F. was given. The case has been followed up for three months and there has been no relapse. The response was similar to that obtained in other megaloblastic anaemias with liver, folic acid, vitamin B_{12}, or penicillin.

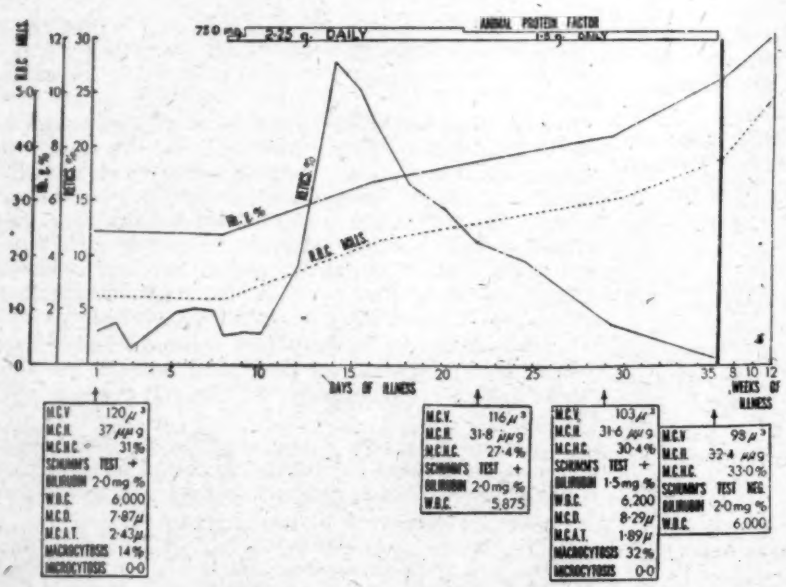
Case History

The patient was a five-months pregnant African about 30 years old, belonging to the Mtita tribe. She was well nourished and of good physique, but said she never ate meat. She entered the King George VI Hospital, Nairobi, on May 1, 1951, for weakness, breathlessness, palpitations, and pains all over the body. She was icteric and obviously ill. There was no oedema of the back or legs. The spleen was 1 (Hackett). The liver was not palpable. The heart showed nothing that was not compatible with her severe anaemia. The chest was normal, and she was afebrile. Her tongue, teeth, and nails were all normal, and she had no nervous symptoms. Free acid was present in the gastric juice after histamine. She had had three previous pregnancies: all the children had died between the ages of 2 months and 1 year. Scanty hookworm eggs were found in the faeces.

Laboratory Examination on May 2 showed: red blood cells, 1,310,000; haemoglobin, 4.9 g.%; haematocrit, 15.7%; reticulocytes, 2.8%; M.C.V., 120 μ^3; M.C.H., 37 $\mu\mu$g.; M.C.H.C., 31.4%; Schumm's test, +; indirect Van den Bergh, 2.6 mg. per 100 ml.; sickling tests, negative; white blood cells, 6,000; sternal marrow (Arikin's method), hyperplastic, many giant stab-cells and intermediate megaloblasts; Price-Jones curve, slightly to right of normal; macrocytosis, 14.2%; microcytosis, 0.0; M.C.D., 7.87 μ; M.C.A.T., 2.43 μ. The rest of the blood findings for her stay in hospital are shown in the Chart.

From May 2 to 9 she was kept under observation and no treatment whatever was given. During this period the reticulocytes fluctuated between 1 and 5.4%. The blood count and haemoglobin fell slightly. On May 9 750 mg. of A.P.F. was given by mouth, and on the following 13 days 2.25 g. (nine capsules daily). During the next 14 days the amount was reduced, owing to short supply, to 1.5 g. daily. Five days after the beginning of treatment there was a great improvement in the patient's appetite and she said she felt much better.

Seven days after the first dose of A.P.F. the reticulocytes rose to 27%, the expected level for the blood count. On May 22 the red cells had risen to 2,192,000, the haemoglobin to 7 g.%, and the haematocrit reading to 25.5%. About this time the patient complained of belly-ache, but otherwise felt well and was walking about. She left the hospital on June 28, with a red-cell count of 3,420,000, a haemoglobin of 10.5 g., and a haematocrit of 35%. Sternal puncture on June 25 showed an active erythroblastic-normoblastic marrow with no megaloblasts or giant stab-cells. The indirect van den Bergh was still 2 mg. per 100 ml., and Schumm's test continued to be positive. She attended as an out-patient on July 5, with a red-cell count of 3,750,000 and a haemoglobin of 10.8 g. On August 28 she again visited us, looking fit, with a red-cell count of 4,440,000 and a haemoglobin of 12 g. Neither the red blood cells nor the haemoglobin reached normal values: we suppose that here, as in Macedonia, the pregnant need treatment continually until the child is born.



Discussion

Animal protein factor has been shown by numerous investigators to be a growth factor for pigs (Cunha *et al.*, 1949), chicks (Stokstad and Jukes, 1950), turkeys (McGinnis *et al.*, 1949), and rats (Piccioni *et al.*, 1951). Penicillin, "terramycin," and "bacitracin" have similarly been shown to promote animal growth and/or reduce mortality in the newborn.

In some groups of animals A.P.F. is stated to produce its growth effects independently of vitamin B_{12}, and several investigators have shown that aureomycin has a "sparing action" on vitamin B_{12} (Stokstad and Jukes, 1951; Cravioto-Munoz *et al.*, 1951). Reid and Couch (1950) failed to obtain growth increases in chicks which were fed A.P.F. that contained vitamin B_{12} but no aureomycin, but growth was increased when the A.P.F. containing *Streptomyces aureofaciens* fermentation products was given. Colby and his collaborators (1952) have found that 100 mg. of aureomycin fed daily to lambs decreased their growth rates, but growth could be stimulated by the addition of the vitamin-B complex. Davis and Chow (1951) have found that aureomycin increases the vitamin-B_{12} activity of faeces in rats and improves their nutritional status, and they suggest, as we did, that the antibiotic is selectively destroying certain micro-organisms which are competing for accessory factors synthesized by other groups of bacteria, or destroying organisms that produce toxins that might be interfering with the utilization of accessory nutrients.

Roine and Elvehjem (1950) have claimed to have improved the growth of guinea-pigs by adding gum arabic, potassium acetate, and MgO to the diet, and suggest that such a diet produces an environment in the caecum in which suitable "growth-promoting" flora can develop. Biely and March (1951) have found that small amounts of aureomycin added to a diet that is suboptimal in nicotinic and folic acids and riboflavin makes such a diet adequate for the growth of chicks. They suggest that this may be due to a reduction in the microflora of the gut which is competing with the host for members of the vitamin-B complex and/or to a proliferation of those micro-organisms which are synthesizing these vitamins (cf. Foy *et al.*, 1951a, 1951b, 1951c).

It has been suggested that the antibiotics that we have used in the treatment of the megaloblastic anaemias have produced their effects by virtue of some unknown haemopoietic factors which they contain, rather than to any effects that they may have on the gut flora. Although this may be the case with A.P.F., as pointed out below, it is not likely to be the case with penicillin. We have found that penicillin will produce its effects in the megaloblastic anaemias only if given in small doses—not more than 200,000 units twice daily by the intramuscular route, and not more than 125,000 twice daily by the oral route. Given in greater amounts than these it is haemopoietically ineffective (Foy and Kondi, unpublished). If the effects of penicillin were due to its content of unknown haemopoietic factors then one would expect results from large as well as small doses.

Our explanation of these facts, provisionally, is that large doses of this antibiotic not only clear the gut of the microflora that is competing with the host for the supply of essential factors but also destroy that flora which is synthesizing these factors. We are aware that increases in the dosage of antibiotics does not necessarily widen their spectrum of action, but variations in bacterial sensitivity are known to exist and to be affected by varying doses of antibiotics. There is also the possibility that the antibiotics may be producing their effects by suppressing a flora responsible for an enterotoxaemia (Sieburth *et al.*, 1951).

If these antibiotics are producing their growth effects by dealing with bacterial flora, the possibility of the production of antibiotic-resistant strains should be borne in mind. This will be particularly the case if small continuous doses are given. It may well be that some of the discrepant results are due to production of antibiotic-fast competitor strains.

The response that we have obtained to A.P.F. in the megaloblastic anaemias of Africans may be due to (1) A.P.F., (2) unknown factors in the A.P.F., (3) the small amount of aureomycin in the A.P.F. acting directly on bacterial flora; or (4) small amounts of vitamin B_{12} contained in aurofax and "spared" by the antibiotic present.

Summary

Megaloblastic anaemia of pregnancy in an African has been successfully treated with animal protein factor. A maximum reticulocyte response was attained on the seventh day of treatment, and was followed by the expected red-cell and haemoglobin regeneration and a return of the bone marrow to normal. No other treatment was given, and the response was similar in every way to that which we have obtained from liver, folic acid, vitamin B_{12}, and penicillin.

It is suggested that the response may have been due to (*a*) changes in the bacterial flora of the gut brought about by the antibiotic present in the A.P.F.; (*b*) an unknown haemopoietic factor present in the A.P.F.; (*c*) the small amount of vitamin B_{12} present in the A.P.F.; or (*d*) "sparing action" of the aureomycin on the vitamin B_{12}.

The failure of large doses of antibiotics to produce a cure in the megaloblastic anaemias would seem to indicate that their effects are not due to their supposed content of unknown haemopoietic factors, but rather to their action on the microflora of the intestine.

Our thanks are due to the Director of Medical Services for permission to publish this paper, and to the Assistant Director of Laboratory Services for innumerable facilities given to us. We again have to thank the medical and nursing staff of the King George VI Hospital, Nairobi, for their continued help in our work.

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Onchocerciasis is found in East and West Africa, the Congo, and South America. The worst area is West Africa, where at present for every five persons with the disease two go blind. This year survey teams are being sent out to West Africa by the British Empire Society for the Blind to tackle the menace of onchocerciasis which is spreading along the river systems there. In the northern territories of the Gold Coast alone 100,000 people are believed to be infected and 40,000 of them are blind. The disease is depopulating the most fertile land—land scheduled for development. A recent report concerning this area tells how an ophthalmic surgeon visiting a village waited for patients to turn up. Eventually a long line of men and women—113 of them—shuffled slowly into view. As they came closer he was appalled to see that they walked patiently in single file, each with a hand on the next person's shoulder, because they were all blind or nearly blind. The British Empire Society for the Blind is confident, however, that further research into methods of elimination of the simulium fly and the testing and development of recently discovered drugs will eventually bring control of the disease. This work is part of the Society's widespread campaign against blindness and eye diseases in which over 20 colonial territories are already participating.

Medical Memoranda

Use of Plasmapheresis in Blood Donors

Our studies on this subject began in May, 1950, because the demand for plasma in our blood bank far exceeded that for packed cells. It seemed a pity to throw away the red cells, which are precisely the portion of blood that requires more time and material for its regeneration. It is known that 100 ml. of blood contains some 16 g. of haemoglobin, a specialized protein whose metabolism is linked with the metabolism of iron, while the same amount of blood contains only 4 g. of plasma proteins, whose regeneration is considered to be both qualitatively and quantitatively much easier. It is also well known that in most cases haemoglobin regeneration is the deciding factor in establishing the safe interval between bleedings of blood donors. To regenerate 100 ml. of whole blood the building material for 16 g. of haemoglobin and 4 g. of plasma protein plus the corresponding amount of iron should be supplied. To regenerate the amount of plasma yielded by 100 ml. of whole blood only the building material for 4 g. of plasma protein should be supplied. There are, of course, many other considerations that make it clear that the production of plasma protein in man should be expected to be much more rapid than haemoglobin production.

METHOD

From May, 1950, to July, 1951, we performed plasmapheresis in over 320 cases. Our experience has led us to adopt the following technique.

At weekly intervals the donor is bled for plasma, using the same apparatus as for blood collection, approximately 400 ml. of blood being drawn into acid-citrate–dextrose mixture. Immediately after the bleeding the red-cell suspension taken the previous week from the same donor is injected by gravity through the same needle, using a drip counter. The whole collection–injection process is thus made with a single venepuncture, and as a rule takes some 8–10 minutes. Shortly after collection the blood is centrifuged, and is kept in this condition in the refrigerator until the following week, when the plasma is removed and the packed cells are suspended in citrate–saline, ready for injection.

As implied, donors are bled for plasma every week—actually the same day each week. We presumed that such a time interval should be more than sufficient for plasma regeneration, and we felt that the reinjected cells could hardly have been damaged by storage. Our expectations have been fulfilled. In two instances we have performed weekly plasmapheresis for about one year with scarcely any interruption. Plasma examinations do not show significant change, and subjectively these plasma donors declare that they feel quite normal throughout.

SELECTION AND EXAMINATION OF DONORS

As a routine, however, we prefer to change our donors as a safety measure after a few months of plasmapheresis. We think this precaution is worth adopting, as we are dealing with a new technique in which there is no experience beyond our own.

We have chosen as our plasma donors those who appear to be in the best physical condition and whose standard of living leads us to expect that plasma regeneration will not be hampered by poor constitution or undernourishment.

Laboratory Examinations.—Every week we perform haemoglobin and total plasma protein estimations. Every month we carry out Wassermann and Meinicke tests and determine the albumin:globulin ratio. So far no donor has had to be rejected for failure to regenerate the plasma protein completely.

Besides the advantage that with plasmapheresis there is no waste of red cells, there are other advantages—for example, easy control of the donor's health and the practically complete exclusion of danger of transmission of jaundice. The method also reduces the number of donors as well as the clerical work, since the donors come automatically at regular intervals, usually once a week.

We have also carried out plasmapheresis in a few pathological conditions. In essential and renal hypertension we have found a striking subjective improvement, which, however, is not matched by a corresponding betterment of the objective symptoms. Thus headache and mental sluggishness disappear, while blood pressure and renal-function tests show little improvement. The use of plasmapheresis in treatment of disease will be the subject of further study.

SUMMARY AND CONCLUSIONS

The first use of plasmapheresis in blood donors is described, with details of the technique employed and of the criteria adopted for the selection and regular examination of plasma donors.

About 200 ml. of plasma may be drawn safely from a healthy person every week for short periods, and perhaps even for longer ones.

Subjective improvements are reported from a few pathological cases.

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Spontaneous Arterial Occlusion During an Epileptic Fit

The development of a spontaneous obstruction in a peripheral artery during an epileptic fit is a rare occurrence. It is therefore of interest to record a case in which the lumen of the left posterior tibial artery became occluded during a major epileptic attack, with subsequent ischaemic cramp in the leg.

CASE REPORT

The patient, a man aged 47, had suffered from attacks of idiopathic major epilepsy for many years. These had been controlled by soluble phenytoin and phenobarbitone tablets, but on April 9, 1950, he had three fits following one after another. When he regained consciousness he found that his left leg was white and lifeless below the level of the mid-calf. There was no sign of any external injury. It was 16 hours before sensation returned to the leg, and the foot remained numb for four days. He then complained that the left foot felt cold and that cramp occurred in the calf and foot when he had walked about 200 yards (183 metres). The pain wore off after resting for a few minutes.

He was first seen at the West End Hospital for Nervous Diseases a month after the onset of the symptoms. The whole of the left foot was then colder and paler than the right. There was no pulsation in the dorsalis pedis artery or in the posterior tibial artery at the ankle. Above the knee and throughout the right leg normal pulsations were felt. The cardiovascular system was otherwise healthy; there was no evidence of peripheral arteriosclerosis, and his blood pressure was 130/85. The blood Wassermann reaction was negative, and no vascular calcification was seen in the radiographs of the legs.

He was treated with Buerger's exercises and was given tolazoline hydrochloride ("priscol"), 25 mg., and nicotinic acid, 100 mg., each three times a day by mouth. The symptoms in the left leg subsequently improved. By September he could walk 300 yards (274 metres) before experiencing cramp in the calf, and could manage to play nine holes of golf. In January, 1951, the foot was warm as far as halfway down the instep, but it was cold beyond this, without, however, any discoloration of the skin. In April he could walk without experiencing any cramp at all and play a full round of golf. The left foot was equal in warmth to the right to within an inch (2.5 cm.) of the base of the toes. There was still no pulsation in either the dorsalis pedis or the posterior tibial artery.

COMMENT

It is assumed that the symptoms referred to in the left leg were the result of a sudden arterial occlusion that occurred during the epileptic convulsions. There are two possible explanations to account for the obstruction. The first is that the convulsions led to the displacement of an atheromatous plaque somewhere in the arterial tree which passed distally and lodged in the left posterior tibial artery. The alternative explanation is that the severe and prolonged contractions of the leg muscles damaged the intimal lining of the artery, with resulting thrombosis. In spite of the absence of objective evidence of peripheral arteriosclerosis, it seems more likely that the symptoms were due to arterial obstruction by a dislodged atheromatous plaque, possibly from the aorta.

I am grateful to Dr. C. Worster-Drought for permission to publish this report and for his advice in its preparation.

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Toxic Hepatitis and P.A.S.

To date, three isolated instances of toxic hepatitis occurring during the course of treatment with *para*-aminosalicylic acid (P.A.S.) have been recorded (Cuthbert, 1950; Hurrell, 1950; Landsborough, 1951). The Medical Research Council Report (1950), which deals with the results of combined streptomycin and P.A.S. therapy, makes no reference to this complication; it therefore seems opportune to present a further case in detail.

CASE REPORT

A 2-para aged 31 was admitted to hospital on September 28, 1950, suffering from active bilateral pulmonary tuberculosis complicated by laryngitis. She had received treatment for pulmonary tuberculosis in a sanatorium in 1945, and remained well until 1950, when pregnancy supervened; she was confined in July of that year. At the time of admission to hospital active lesions involved the upper and mid-zones of both lungs, and there was advanced tuberculous infiltration with ulceration of the vocal cords and epiglottis.

Routine treatment was prescribed, and streptomycin dihydrochloride, 1 g. in divided daily doses, and sodium P.A.S., 15 g. daily, were given from October 3 until November 8. On October 31 the patient developed a rise in temperature, with rigor and sickness, and eight days later a generalized scarlatiniform erythema with gross oedema of the face was observed. Streptomycin and P.A.S. (total dosage 540 g.) were then stopped, and mepyramine hydrogen maleate ("anthisan"), 1 g. thrice daily, was administered. This was discontinued in favour of diphenhydramine hydrochloride ("benadryl"), 300 mg. a day, as from November 15.

On November 16 the temperature was 103° F. (39.4° C.), and she continued to be febrile for a further period of 18 days, fever being accompanied by rigor, sickness and diarrhoea, and albuminuria. Jaundice developed on November 18, became pronounced within a few days, and was accompanied by mental confusion and hallucinations.

A blood examination on November 17 showed: leucocytes, 12,500 (polymorphs 40%, lymphocytes 50%, monocytes 7.5%, basophils 2.5%). The plasma bilirubin content was 6.5 mg. per 100 ml.; blood urea, 30 mg. per 100 ml.; prothrombin time, 41 seconds (control 19 seconds); blood level of P.A.S., 0.52 mg. per 100 ml. Blood culture was sterile and W.R. negative.

Despite the evidence of hepatic dysfunction, streptomycin was restarted and was continued without further interruption until January 13, 1951 (total 94 g.), but P.A.S. was not again given, since, in the opinion of one of us (A. G. F.), it had been the probable cause of both the toxic erythema and the hepatitis. Lead acetate lotion was applied to the face and ung. oleum eucalypti to the remainder of the body.

Blood examination on November 22 showed: serum proteins, 5.75 g.% (albumin 1.6 g., globulin 4.15 g.); alkaline phosphatase, 39.5 units; bilirubin, 12.5 mg. per 100 ml.; thymol turbidity, 9 units. On November 25 jaundice was still present and the liver was moderately enlarged and palpable below the costal margin. One week later the generalized erythema had almost completely faded, and a fine branny desquamation was observed. The jaundice was subsiding, and the patient seemed to have improved, her mental attitude being much brighter. By December 8 both jaundice and erythema had cleared; the local treatment was now discontinued, and benadryl was gradually withdrawn.

Blood examination on December 6 showed: serum proteins, 6.25 g.% (albumin 3.6 g., globulin 2.65 g.); serum bilirubin, 1.8 mg. per 100 ml.; alkaline phosphatase, 16.4 units; thymol turbidity, 7 units; and on December 27 serum proteins 8 g.% (albumin 4.4 g., globulin 3.6 g.); alkaline phosphatase, 18.3 units; bilirubin, 0.6 mg. per 100 ml.; thymol turbidity, 8 units.

At the time of discharge from hospital, on June 1, the patient's general condition was satisfactory; she felt well and had gained weight. Radiological examination showed the pulmonary lesions in the upper zones to have become inactive; sputum had been tubercle-negative on three consecutive monthly examinations, and the tuberculous laryngitis was found to have healed. Over a month later she was still apyrexial and symptomless, and there had been no recurrence of rash: sputum was tubercle-negative, and the *x*-ray appearance of the lungs was unchanged.

DISCUSSION

The pathogenesis of this hepatic dysfunction is still obscure, and in consequence the evidence that P.A.S. caused a toxic hepatitis can only be presumptive. Nevertheless, a search for other possible causal factors, including contact infection, was unsuccessful.

Features peculiar to this patient, which differ from previous reports and are worth special mention, include:

(1) The widespread scarlatiniform character of the rash, associated with fever and collapse. Hitherto the sensitization rashes noted and described in association with P.A.S. therapy have most often been of morbilliform type, and there seems to be some evidence that untoward cutaneous reactions to P.A.S. are due to its salicyl radical (Horne, 1949; Kierland and Carr, 1949). Eruptions due to ingestion of salicylates are usually either scarlatiniform or morbilliform erythemata.

(2) Despite the gravity of her tuberculosis and the serious nature of the hepatitis she not only survived but was much improved on discharge from hospital, the tuberculous lesions having apparently healed. Of the other cases previously reported one died and two recovered.

(3) The total dosage of P.A.S. given was 540 g., dosage until the onset of symptoms being 435 g. (Cuthbertson gave 800 g., Hurrell 163 g., and Landsborough 270 g. until the onset of symptoms, total dosage 465 g.). It would appear that reaction is due to individual idiosyncrasy rather than to overdosage with P.A.S.

Acknowledgment is made to Dr. M. A. Foulis, medical superintendent, Robroyston Hospital, Glasgow, for permission to publish this report.

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Reviews

MIND AND THE WORLD

Mind, Perception, and Science. By W. Russell Brain, D.M., F.R.C.P. President of the Royal College of Physicians of London. (Pp. 90. 6s.) Oxford: Blackwell Scientific Publications. 1951.

In the introduction Sir Russell Brain states as the thesis of this book "that it is possible to accept all the new knowledge which neurophysiology and psychology can provide and yet preserve the mind's autonomy in its own sphere." That is a very arresting statement to make at a time when we are assailed by so many assertions to the contrary, assertions which are also claimed to be based on the "new knowledge." Sir Russell Brain's philosophical position of dualism is virtually indistinguishable from that of Sherrington and is likewise based on a very clear understanding of the role of neurophysiological events in perception. An attractive feature of the book is the effective use that is made of concrete illustrations in the argument, which is thus given a lucidity that is as unusual as it is welcome in this perplexing field.

Chapters 4, 5, and 6 make particularly good reading, and, in his deft handling of the concepts of "perceptual world" and "physical world," Sir Russell Brain has made an important contribution that should clear up many old controversies and confusions in the field of perception. To some extent Chapter 1 is also on the same theme, but was written several years earlier, and is much less satisfactory. The criticism of physiological idealism is not convincing and in fact is largely answered in Chapters 5 and 6, where it is shown that physiological idealism can be developed so that such a process as projection becomes intelligible. Comparison of the first with these later chapters gives a measure of the progress that Sir Russell Brain has made, and gives hope that we may expect further valuable contributions from him. In particular one hopes that his success with perception will tempt him into the field of will, the "I-doing" of Sherrington.

The last chapter, on the "Status of Mind," is in the form of a dialogue between author and reader, and gives the author a chance to develop some new arguments and in particular to attack the views that Professor G. Ryle develops in his book *The Concept of Mind.* Again one is impressed by the effectiveness with which some philosophical arguments are demolished by reference to the neurophysiological processes concerned in perception.

In conclusion, this book is strongly recommended to all who take an intelligent interest in the problems of the nature of man and his relationship to the world. It can be read by those who have no technical knowledge of neurology.

J. C. ECCLES.

WORLD FOOD SUPPLIES

Four Thousand Million Mouths. Edited by F. le Gros Clark, M.A., and N. W. Pirie, M.A., F.R.S. (Pp. 222. 12s. 6d.) London: Oxford University Press. 1951.

The present population of the world stands at 2,300m., and with an increase of about 1% annually the time does not seem far distant when food will have to be found for 4,000m. mouths. The purpose of this book is to draw attention to the alarming problem which may confront many of the rising generation, and to collect together the opinions of experts on methods by which the production of food may be increased. At the same time most of the contributors emphasize that an increased supply of food can be only a temporary palliative unless accompanied by some form of birth control. This in turn would seem impracticable until the vast illiterate masses in various parts of the world have been sufficiently educated to appreciate their social responsibilities, and so to avoid having more progeny than can be adequately supported under the economic conditions in which they live.

F. le Gros Clark contributes an excellent and well-balanced account of the theories of Malthus, a West Country cleric and lecturer in economics who foresaw the present problem at the end of the eighteenth century; his gloomy prophecies were falsified, or at least postponed in their fulfilment, by the Industrial Revolution and the opening up of the wheat-growing prairies of North America. G. V. Jacks writes on conserving the soil, F. Yates on manuring for higher yields, F. C. Bawden on growing healthier crops, and S. C. Harland on genetics and the world's food. H. D. Kay considers the importance of milk, and the measures necessary to improve supplies are discussed, and John Hammond discusses the pig as a producer of food. C. E. Lucas next writes on the catching of fish, and the possibilities of fish farming, and G. A. Reay and C. L. Cutting on the preservation and use of fish. Two interesting articles by N. W. Pirie on the circumvention of waste and by A. L. Bacharach and T. Crosbie Walsh on the processing of food conclude the work. In general, the standard of the contributions seems well worthy of the spirit of scientific humanism which the authors hope will eventually dispel the shadow of world hunger.

T. MOORE.

INHERITANCE OF BLOOD GROUPS

Human Blood Groups and Inheritance. By Sylvia D. Lawler, M.D., and L. J. Lawler, B.Sc. With a foreword by R. R. Race, Ph.D., M.R.C.S. (Pp. 85. 3s. 6d.) London: William Heinemann. 1952.

Under the heading of "blood groups" an ever-increasing amount of knowledge is accumulating. Only a little of this knowledge is of direct concern to clinicians, and only some of the facts are of interest to serologists, to anthropologists, and to geneticists; each group of workers needs a special account. Certainly no one person is likely to want to be familiar with the whole body of knowledge. The present short book dwells chiefly on the genetical aspects and has been "designed for the biology student and the interested lay reader." As its title makes clear, it is exclusively about human blood groups, and it is thus not quite fair to complain that the book might have been even more useful to the biology student if it had included a chapter on blood groups in animals. For example, presumably the biologist would be interested to know that a chemical substance similar to the human blood group factor A occurs in numerous other species. With this possible limitation the book succeeds most admirably in explaining the chief features of blood groups. The authors assume that the reader will have almost no knowledge of scientific terminology and succeed in making clear such words as "allelomorph" and "linkage."

The attempt to make simple generalizations occasionally leads to rather misleading statements. Thus, in writing of iso-immunization to A and B during pregnancy, the authors state that "the rise in titre does not harm the baby." This is bound to suggest to the reader that haemolytic disease of the newborn is never caused by ABO incompatibility, which is not the case. But such passages are few; far more often the authors skilfully succeed in making accurate simplifications, and the book is very easy to read. It can be warmly recommended to the medical reader who wants an elementary account of the inheritance of blood groups.

P. L. MOLLISON.

BIOPHYSICS

Progress in Biophysics and Biophysical Chemistry. Edited by J. A. V. Butler and J. T. Randall, F.R.S. Volumes 1 and 2. Volume 1, pp. 275, illustrated, £2 10s. Volume 2, pp. 322, £2 10s.) London: Pergamon Press. 1951.

These are the first two of a projected series of volumes containing up-to-date reviews of various aspects of bio-

physics. The modern interest in isotopes has determined the inclusion of three essays: one, by Loutit, discussing man's tolerance to irradiation; one, by Sinclair and Lamerton, on the clinical use of isotopes; and a more academic review by Gray on the general biological actions of ionizing radiations. The modern approaches to the elucidation of the structure of living matter are also well discussed. Rudall gives a lucid account of the results of *x*-ray and electron-microscopical studies on proteins, and Preston a similarly enjoyable review of the structure of plant fibrils. Wyckoff describes recent electron-microscopical studies of bacteriophage and viruses. Swann and Mitchison have written a rather polemical (and valuable on this account) critique of recent polarization-optical measurements on cell membranes. Hughes provides an all-too-brief account of phase-contrast microscopy, and Philpot, Engström, and Oster have written highly technical articles on local refractometry, the use of *x* rays in biological assays, and the scattering of light and *x* rays respectively. Crane and Wyke discuss bioelectricity and nervous activity in two long articles. Finally, Gutfreund discusses the properties of solutions of large molecules; Pirenne elaborates, in a very interesting manner, his application of quantum principles to vision; Pryor examines the application of the principles of rubber-like elasticity to the contraction of muscle; and Jordan gives a technical and thorough account of the physico-chemical properties of the nucleic acids.

The volumes will be immensely useful to research workers in the biological sciences, and the editors are to be congratulated on their choice of subjects. All the contributors deserve praise for the erudition of their articles, although some must be censured for insufficient attention to intelligibility. When an author is discussing a subject requiring real intellectual effort on the part of the reader, it is desirable that his grammar, and necessary that his punctuation, be correct. A phrase such as "but the generation and measurement of the radiation is difficult" is bad grammar. And, because of the absence of punctuation, a sentence such as the following is unintelligible at first reading: "For small optically isotropic scatterers the intensity of scattering is proportional to $1+\cos^2\theta$ where θ is the angle between the observer and the proceeding incident beam so the scattering is symmetrical about 90° to the incident beam." The task of an editor is unenviable, and the critic who reads the printed article is unaware of the toil that may have converted an originally unintelligible manuscript into tolerable English; one hesitates, on this account, to blame the editors of these volumes for the many solecisms of this sort that may be found in some of the articles under review. But from the following crime, taken from their preface, they cannot be absolved: "We hope that as it develops both the occasion and opportunity of including reviews of the progress of this method will arise." A comma might make the sentence intelligible, but no amount of punctuation would make it good English.

HUGH DAVSON.

HAEMOLYTIC DISEASES OF CHILDREN

Die Hämolytischen Syndrome im Kindesalter. By Dr. Conrad Gasser. (Pp. 308; 101 illustrations. M. 45.00.) Stuttgart: Georg Thieme. 1951.

Possibly the best-known advance in haematology in the last 10 years is concerned with the blood antigens and their part in the production of icterus gravis. How much other, less spectacular, knowledge is accruing may be glimpsed from this monograph on the haemolytic diseases of infants and children. Writing from the Zurich Children's Hospital, Dr. Gasser has at his disposal a vast wealth of clinical material, and from a study of his own personally observed and carefully investigated cases he has written a book which is a model of its kind. It will be read with profit by all interested in the haemolytic diseases of children.

After a short account of the normal production and destruction of the red cell the author discusses the specific anaemias, grouped roughly into those produced by toxins, those due to antibodies of one sort or another, the haemolytic syndromes accompanying a constitutional defect of the red cell, and finally the symptomatic haemolytic anaemias. Summaries of illustrative cases are included throughout the text, and the many graphs of the salient haematological data are excellent. The book is produced on very good paper, so that the photographs have a chance to show their worth, and there is an adequate bibliography.

I. A. B. CATHIE.

PUBLIC HEALTH IS PEOPLE

Public Health is People. By Ethel L. Ginsburg. (Pp. 241. 14s.) New York: The Commonwealth Fund. London: Geoffrey Cumberlege. 1950.

This is a report of what happened in a fortnight in July in 1948 at Berkeley, California. Sixteen psychiatrists, paediatricians, and public health leaders acted as "faculty" to a "student body" of thirty health officers drawn in the main from the cities and counties of the State of California. Mechanical recording was freely used, and Mrs. Ginsburg has undertaken the enormous task of rendering down a great mass of material and presenting the result in a book of reasonable compass. And the result is excellent. Apparently there are still some people who imagine that public health is sanitation: here it is vividly demonstrated that public health is people. The main theme discussed at this study group was the application of our knowledge of mental health to the organization of the general public health service.

This book is instructive, practical, and entertaining. It contains a plea for a more sympathetic approach to the ordinary man and a correspondingly better understanding of his virtues, vices, and needs. It deals in psychosomatic medicine with a less resounding title—and all the better for that. This delightful book will appeal to all those who work in the field of community medicine and to many who do not but who also are interested in people. The author is to be congratulated on her success in providing us with a well-arranged and well-balanced report of an important social study of great interest.

C. METCALFE BROWN.

PHYSIOLOGY FOR STUDENTS

Human Physiology. By C. C. Chatterjee, B.Sc., M.D.(Cal.). (Pp. 813; 141 figures. £2 5s.) Calcutta: U. N. Dhur and Sons. 1951.

This is a textbook of physiology by a former member of the department of physiology at the Medical College of Calcutta University. It was written, as its name implies, with a view to teaching physiology of the human subject. It therefore embraces within its covers the essentials of histology, biochemistry, and biophysics. At no stage does it pretend to be a book suitable for the honours or postgraduate student. It is almost entirely devoid of references to original papers. On the other hand, it is well written in good English and is comprehensive. The author reviews the evidence for the phenomena and findings of physiology in a lucid and successful manner, and he illustrates the physiology by referring to the pathological conditions which show the extremes of physiology. Plentiful footnotes explain the terms used. The student is given alternative theories on unsettled points. There is a tendency, not excessive, to group the story under headings rather than as a literary venture in continuous essay form.

It will be a useful book for the type of student who likes his reading systematized for him, and especially for anyone sitting for the second medical examination who is revising his work. But it is more than a mere "cram" book: it is a brave venture to get physiology, including the advances of the post-war years, within one cover for the undergraduate student, despite a somewhat dogmatic approach.

A. ST. G. HUGGETT.

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THE NEW CHEMOTHERAPY FOR TUBERCULOSIS

That a new type of drug had been found to exert a remarkable effect in tuberculosis was first announced in the lay press in February last. A series of six papers in the April issue of the *American Review of Tuberculosis* (1952, **65**, pp. 357–442) now makes it possible to assess the importance of this discovery. All the work described is recent and some of it incomplete, and there are several addenda reporting a few weeks' further progress in animals or patients, but the evidence is enough to suggest that a striking advance has been made.

The two drugs whose action has been under study are hydrazides of nicotinic acid, and it seems that their antituberculous activity was observed independently at the Squibb Institute for Medical Research and the scientific laboratories of Hoffmann-La Roche. They are *iso*nicotinic acid hydrazide ("nydrazid," Squibb; "rimifon," Roche) and 1-*iso*nicotinyl-2-isopropyl hydrazine ("marsilid," Roche). The former in a concentration of 0.02 μg./ml. inhibits *in vitro* the growth of *Myco. tuberculosis* (an activity at least five times that of streptomycin); the latter inhibits in a concentration of 1.6 to 3.1 μg./ml., and both are slightly less active in medium containing serum. A fivefold increase in resistance of the bacillus to the *iso*propyl compound has been observed after seven fortnightly transfers, and an addendum to a paper by W. Steenken and E. Wolinsky records the disturbing fact that growth eventually appeared in cultures containing 25 μg./ml. of *iso*nicotinic acid hydrazide (that is, 750 times the initial inhibitory concentration). It is evidently not yet known whether acquired resistance is temporary or permanent, and it has not so far been observed *in vivo*, but the distant future of the treatment evidently depends very largely on these two points. Action on other bacteria is not discussed, but it seems that no other species is susceptible to concentrations of the same order, and bio-assay has therefore to be conducted with a culture of *Myco. tuberculosis* itself. Fortunately *iso*nicotinic acid hydrazide can be assayed chemically in body fluids, and D. F. Elmendorf, W. U. Cawthon, C. Muschenheim, and W. McDermott have shown that the two methods give roughly concordant results, and have used mainly chemical assay in a pharmacological study in man. After an oral dose of 3 mg./kg. body weight the plasma concentration rises to 1.3–3.4 μg./ml. and diminishes little up to the sixth hour; the subsequent fall is also slow, and, although none of the substance may be detectable by the method used after 24 hours, it can be deduced from studies of urinary excretion that a therapeutically useful concentration persists for this length of time. The usual practice has in any case been to give two or three doses daily. The drug appears in the cerebrospinal fluid in adequate concentrations: indeed, according to table 9 of these authors' paper the concentration in the cerebrospinal fluid may slightly exceed that in blood taken at about the same time. Of nine patients so studied, five had active tuberculous meningitis, but owing to differences in dosage between these and the remainder it is not possible to decide whether the existence of meningitis affects the drug concentration in the fluid. Although most of the drug is excreted in the urine, it has also been found in saliva, faeces, and in one specimen of pleural exudate: technical difficulties precluded its assay in sputum.

Therapeutic action against experimental tuberculosis is reported in two of these papers. J. Bernstein and his colleagues tested *iso*nicotinic acid hydrazide in mice inoculated intravenously with the Ravenel strain of bovine tubercle bacillus, giving the drug either in the diet or subcutaneously. P.A.S. (*para*-aminosalicylic acid) and streptomycin were also tested for comparison, and the superiority of the new drug, under the conditions of this experiment, is particularly evident when treatment was delayed seven or even fourteen days after inoculation, giving 10/10 and 7/9 survivors respectively, whereas the corresponding score of streptomycin was 0/10 and 0/10. P.A.S. gave no survivors and prolonged life by only a few days, even when administered *ab initio*. Steenken and Wolinsky used 1-*iso*nicotinyl-2-isopropyl hydrazine, administered in most cases intramuscularly, for the treatment of tuberculosis in guinea-pigs and rabbits. In these two species experimental disease produced by intracerebral and intravenous inoculation which was uniformly fatal in 3 and 3–6 weeks respectively was regularly suppressed, all animals surviving throughout the period of treatment, which was 60 and 71 days. Recurrences some weeks later were being observed when this paper was written, and

subinoculations from guinea-pigs (infected subcutaneously) in which the disease was also apparently suppressed showed that the infection was not eliminated. An interesting point is that the treatment also suppressed skin reactivity to tuberculin.

The main item of clinical evidence is a paper by E. H. Robitzek and I. J. Selikoff, of the Sea View Hospital, Staten Island, New York, where these drugs have been in use since October last. It seems that most of the 97 patients treated were given the isopropyl compound, but six are recorded as having received *iso*nicotinic acid hydrazide. Dosage of each was initially 2 mg./kg. body weight daily, increased to 4 mg. when the lower dose proved to be well tolerated. The report deals chiefly with 44 of these patients, in each of whom bilateral pulmonary disease "had progressed so far that he was no longer a candidate for any other standard accepted form of therapy." They had been under observation for adequate periods: 41 had had from one to five courses of streptomycin and 39 treatment with P.A.S. All had fever, mainly in the higher ranges, and particulars of weight loss, radiological and sputum findings, and other clinical features provide assurance that they were "hopeless" cases, "in many instances close to terminal status." Of six patients whose history is given in detail, four were young Negro females, in whom the prognosis of such a form of the disease is particularly bad. It seems to be no exaggeration to say that the immediate effect of treatment was dramatic. Fever subsided, temperature almost always reaching normal in ten days and sometimes in two: there was "a sharp return in sense of well-being," a voracious appetite developed, and rapid weight gain followed. In the last connexion the authors refer to their "belated observation . . . that in many instances the doses were spontaneously diminishing. A weight gain of 50 lb. (22 kg.) in a 100-lb. patient automatically reduces the dose by 33⅓%." Although several patients did gain weight to about this extent the average gain after 4 to 15 weeks' treatment was 16.5 lb. (7.5 kg.) in males and 22 lb. (10 kg.) in females. Diminution in cough and sputum, and in the numbers of bacilli in the sputum, regularly began in the second week: in addition to a shift from large volumes of sputum with a high Gaffky count to small volumes with a low count, it is recorded that eight patients became repeatedly sputum-negative (by film only). Improvement in *x*-ray appearances included the apparent closure of single or even multiple cavities. Laryngitis, glossitis, and (presumed) enteritis were relieved, and several women menstruated within a few weeks after months of amenorrhoea. These findings and those in mice almost moribund before delayed treatment suggest that these drugs may prove to exert their most striking effect in severe and extensive disease: evidently at least the ordinary rules for other forms of chemotherapy do not apply to them. In view of such results the authors' final conclusion that "further investigation of the hydrazine derivatives of *iso*nicotinic acid is warranted" seems an understatement, but it is true that many questions relating to this treatment remain to be answered, in particular those of its long-term effects. Elmendorf and his colleagues do not record the therapeutic effects in the patients in whom they made their pharmacological studies, and their associates in Arizona are still pursuing a study of the treatment of meningeal and miliary disease in Navajo Indians.

No serious toxic effects have yet been observed. Twitching of the extremities and exaggerated deep reflexes are common, and may or may not represent the same effect as that produced in animals by lethal doses, which evidently act mainly on the nervous system. Constipation, vertigo, and difficulty in starting micturition have also been noted. There are two papers, by W. M. Benson *et al.* and B. Rubin *et al.*, on toxicology in animals. It is interesting that the lethal dose in mice is almost the same by the oral and four parenteral routes, since it indicates that absorption from the alimentary tract must be nearly complete. The maximum daily repeated doses of *iso*nicotinic acid hydrazide tolerated by mice, rats, and dogs are 64, 40, and 10 mg./kg., and it is suggested that the body-weight/surface-area ratio may thus be used to calculate tolerance. If this assumption is correct and inter-species differences are not dependent on factors varying in other ways the dose of 4 mg./kg. now being used clinically is near the maximum. The effects observed in dogs given toxic doses repeatedly include anorexia, weight loss, tremors, ataxia, jaundice, and anaemia. Post-mortem findings were fatty change in the liver and gross changes in various organs (no microscopical data) which suggest that the anaemia must have been haemolytic.

Such findings as these indicate the need for considerable caution. Optimum dosage and duration of treatment, the relative merits of the two drugs, and the possibility of acquired bacterial resistance all remain to be determined. Everyone will therefore agree, at least in principle, with statements issued in this country by the Ministry of Health, and across the Atlantic by the American Trudeau Society, that this treatment should for the present be given only to patients in institutions where there are full facilities for detecting possible toxic effects as well as for assessing results. Whether it will be possible so to

restrict its use for more than a very short time is another matter. These drugs are not like newly discovered antibiotics, the production of which is at first on a very small scale. They are simple compounds, easily manufactured. They are also easily administered, so that to the prospect of indiscriminate prescription has to be added even the possibility of self-medication. The only type of case in which their effect has so far been recorded is just that—the "hopeless"—on whose behalf demands will be most immediate, insistent, and urgent. We have therefore another situation, in a series which began with penicillin, where the distribution of a new drug must be the subject of serious anxiety and, it is to be hoped, well-considered control.

A.C.T.H. AND CORTISONE IN INFECTIVE HEPATITIS

The treatment of infective hepatitis is still far from satisfactory, and it is not surprising that both A.C.T.H. and cortisone have been tried in this condition. With any disease whose course is so variable and whose outcome so unpredictable as infective hepatitis it is difficult to assess the value of a new treatment unless a large series of adequately controlled cases is investigated. So far no such series has been reported on, though some interesting observations have been made. The most promising results were obtained by Webster.[1] Nine cases of hepatitis, including one of homologous serum jaundice and two of arsenical hepatitis, all of which were severely ill despite modern therapy, were treated with aqueous or oily extracts of adrenal cortex. Recovery in all was described as dramatic, and none had any signs of liver dysfunction when examined a year later. Encouraging reports have also come from Colbert and his colleagues,[2] who treated five acute cases of hepatitis with A.C.T.H. given by six-hourly injections of 25 mg. All five rapidly lost their anorexia and developed voracious appetites. Of perhaps still greater importance from the patient's point of view was the disappearance of pruritus, which can prove a most distressing symptom. A prompt fall in serum bilirubin was also recorded, but no definite change in liver size or tenderness. Most significant, perhaps, in relating these improvements to the effect of A.C.T.H. was a definite rise in the serum bilirubin in two cases when the injections were stopped, and a further fall when the treatment was restarted.

A less encouraging picture was drawn by Holmes and Percefull.[3] In a group of patients being treated for a variety of diseases they studied the effect of cortisone therapy upon the results of a series of liver function tests, and while they found no impairment of function attributable to the hormone they also saw no improvement in the two cases of hepatitis included in their series. In view of what is known of the effect of A.C.T.H. and cortisone upon protein, fat, and carbohydrate metabolism, and especially of the ease with which fatty infiltration of the liver is induced in the livers of animals treated with these hormones, it is both surprising and gratifying that no obvious adverse effects result from their use in hepatic disease. The liver plays an important part in the metabolism and inactivation of the adrenocortical hormones. Some steroids—oestrone, for example—are certainly inactivated in the liver, and evidence of hyperoestrinism can and does arise in some cases of hepatitis. Not so much is known about the metabolism of cortisone, but the unusual incidence of side-effects in all five of Colbert's cases strongly suggests that the normal inactivating mechanisms were here at fault.

Virus hepatitis is in the main a relatively benign disease. Two complications are to be feared—acute yellow atrophy, which is usually rapidly fatal, or the development of a chronic condition leading to cirrhosis. The incidence of acute yellow atrophy and the mortality in most epidemics are about 0.2 to 0.5%. To assess the value of a therapeutic agent by its effect upon mortality would therefore require a truly enormous controlled investigation. The incidence of chronic hepatitis, and its sequel cirrhosis, is probably higher than the mortality from acute yellow atrophy, but chronic hepatitis is much less readily identified. Consequently the great majority of investigators attempting to assess the value of any therapeutic agent in infective hepatitis have relied upon the timing of some well-defined clinical event, such as the duration of biliuria or raised serum bilirubin. Until a similar trial is undertaken with A.C.T.H. or cortisone it will be impossible to assess the value of any of these substances in the treatment of hepatitis. From the preliminary results already reported on small and uncontrolled series it can be safely concluded that the therapeutic activity of these new drugs is not remarkable and that an unusually large number of side-effects may be expected.

[1] *Ann. intern. Med.*, 1950, **33**, 854.
[2] *New Engl. J. Med.*, 1951, **245**, 172.
[3] *Ann. intern. Med.*, 1950, **33**, 608.

THE MECHANISM OF TASTE

Ever since the discovery of the taste buds nearly a hundred years ago, and the demonstration of their connexion with the glossopharyngeal nerve, they have been assumed to be the organs responsible for the sensation of taste. Taste buds in man are distributed mainly in the vallate fungiform and foliate papillae of the tongue

and never in the filiform papillae. The vallate papillae are mostly concentrated in a V-shaped area at the back of the tongue, with the apex of the V pointing backwards. Single taste buds also occur elsewhere, in the epithelium of the tongue itself or in the lining of the pharynx, in the palate and the epiglottis. Those which are associated with the papillae are, in the adult, present in the sides, never on the top of the papillae. In infants, however, there may be taste buds in this position on the top, and there are many more of them scattered through the buccal cavity, but they are lost as the child grows. There is no explanation for this diminution in numbers of buds with age.

The buds themselves are made up of two types of cells, which are referred to as "sustentacular" or supporting cells, and rod, hair, or gustatory cells. The former completely enclose the bud rather like the staves of a barrel, but they also occur in the inner part of the bud, where they are mixed with the gustatory cells. Although many workers were of the opinion that these cells were separate entities, Heidenhain,[1] among others, found all stages of gradation between them, and was convinced that they represented the one system of cells. There is a plexus of nerve fibres in the connective tissue beneath these buds, but surprisingly few fibres actually pass into the taste bud itself (intragemmal fibres), where they make contact with both types of cells. Most ramify in the epithelium around and adjacent to the buds (inter- and peri-gemmal fibres). The gustatory cells bear on their distal surfaces a single ciliary process sticking into the gustatory pore which opens to the exterior.

The method whereby this complicated cellular mechanism functions in taste is not known, but recent work by Baradi and Bourne offers a possible explanation. In 1948 Bourne[2] showed by histochemical methods that a phosphate-splitting enzyme (alkaline phosphatase) was located either in the taste buds or in the epithelium covering them in rabbit, bat, monkey, and man. Baradi and Bourne[3] subsequently carried out studies on the rabbit's papilla foliata, which is rich in taste buds, and found six phosphate-splitting enzymes in this region, together with an esterase (an enzyme which splits simple esters) and lipase (an enzyme which splits long-chain fatty acids). By adding small quantities of substances with well-defined tastes to the substrate mixtures used in demonstrating these enzymes, they secured inhibition of the activity of some of these enzymes and enhanced activity of others. This led them to suggest that the mechanism of taste depends upon the differential inhibition or stimulation of enzyme systems in the taste buds and the neighbouring epithelium. Since so many of the enzymes are concentrated not in the taste buds but in the epithelium near them, and since this epithelium is richly supplied with nerves, Baradi and Bourne have suggested that perception of taste is not wholly a function of the taste buds but is partly a function also of this epithelium. This idea is taken further by the anatomical and clinical observations of Dr. Wilfred Harris in his article in our opening pages this week. He finds that lesions of the fifth cranial nerve may impair the sense of taste, which is usually ascribed only to the seventh nerve, and he believes that tactile, painful, and thermal stimuli from the tongue and palate also contribute to form the individual's taste judgments.

Baradi and Bourne point out that the enzymes they studied are distributed in six different sites in and around the taste buds. Since any of the enzymes in these sites is capable of being inhibited, accentuated, or unaffected by a particular tasting substance, and since this can happen in any one of the six sites, it means that each substance being tasted can produce a particular pattern of nerve stimulation according to what it does to a particular enzyme in a particular site. (Enzyme activity in the neighbourhood of a nerve fibre is assumed to cause a nerve impulse.) It can be worked out that this mechanism can thus produce 2,160 different nerve patterns, in other words it can be used to appreciate that number of different tasting substances—a hypothesis that would make the old conception of four basic tastes out of date.

This mechanism can also explain why substances of widely differing chemical nature can have the same or similar tastes. Since the distribution of many of these enzymes overlaps, inhibition (or otherwise) of different enzymes at the same sites by different substances will have the effect of producing the same pattern of nerve impulses which the brain will interpret as the same taste. It is of interest that these enzymes are also present in the olfactory mucosa, a fact which supports the conception of the similarity between taste and smell.

[1] *Arch. mikr. Anat.*, 1914, **85**, 305.
[2] *Nature, Lond.*, 1948, **161**, 445.
[3] *Science*, 1951, **113**, 600; *Nature, Lond.*, 1951, **168**, 977.

AMINE OXIDASE

The earlier physiologists recognized that the sympathetic nerves, which accelerate the heart and mobilize our bodily resources for "fight or flight," are generally opposite in function to the parasympathetic, which adjust our secretions and call forth the responses appropriate for the more pleasurable activities of eating and repose. Sir Henry Dale brought the vegetative nervous system into sharper definition with his brilliant concept of the division into groups of adrenergic and cholinergic nerves, which transmit their impulses to the muscles and glands by liberating the specific transmitter substances adrenaline and acetylcholine respectively. That gave a rational explanation of the selective action of atropine, which blocks the access of acetylcholine to the end-organs in the glands, thereby inhibiting salivation and drying the tears. It also explained the curious anomaly of the sweat glands, which are innervated by nerves derived anatomically from the sympathetic nervous system but which respond to acetylcholine, since these nerves are cholinergic in function.

The story of parasympathetic nervous activity was extended by the discovery of cholinesterase, an enzyme that destroys acetylcholine liberated at the cholinergic

[1] Blaschko, H., Richter, D., and Schlossmann, H., *Biochem. J.*, 1937, **31**, 2187.
[2] Richter, D., ibid., 1937, **31**, 2022.
[3] *J. Physiol.*, 1938, **94**, 87.
[4] *British Medical Journal*, 1952, **1**, 784.

nerve endings, thereby controlling the responses of the organs supplied by these nerves. The effects of cholinesterase inhibitors such as eserine and "prostigmine" could be attributed to their preventing the destruction of acetylcholine: these drugs thus mimic the effects of stimulation of the parasympathetic nerves. That raised the question whether there is a corresponding enzyme that destroys the transmitter substance of the sympathetic nerves. The first evidence that such an enzyme might in fact exist was obtained by a group of Cambridge workers, who showed that the tissues contain an amine oxidase that inactivates adrenaline by oxidizing it in the side-chain to form methylamine and an aldehyde.[1 2] They showed further that this enzyme is inhibited by ephedrine; and their suggestion that the amine oxidase might act physiologically by destroying the transmitter substance at the adrenergic nerve endings received important support from the work of Gaddum and Kwiatkowski,[3] who found that ephedrine increased the constrictive effect of sympathetic stimulation on the arterioles of the rabbit's ear.

It is now known that the sympathetic transmitter substance is not adrenaline, but that it consists mainly of a closely related substance *nor*adrenaline (which is adrenaline minus the methyl group). This has helped to clear up certain anomalies that previously prevented acceptance of the view that the amine oxidase destroys the sympathetic transmitter. Burn and his colleagues have shown that *nor*adrenaline is inactivated more rapidly than adrenaline by the amine oxidase, and they have now collected an impressive array of evidence (summarized in last week's *Journal* by Professor Burn[4]), all of which supports this view of the function of the amine oxidase in relation to sympathetic activity. The amount of amine oxidase in the tissues decreases after denervation, and this can explain the observed changes in the sensitivity to *nor*adrenaline. The amount of enzyme in the blood vessels and in the liver varies with changes in thyroid activity and in such a way as to give a feasible explanation of the greater sensitivity of thyroid-treated subjects to the hypertensive and hyperglycaemic effects of adrenaline. These observations point to the importance of amine oxidase in the control of the blood pressure and indeed in all the functions mediated by the sympathetic nervous system.

PULMONARY TUBERCULOSIS AND PREGNANCY

In recent years many authors have expressed the view that pregnancy has very little effect on the course of pulmonary tuberculosis in the mother. The swing of the pendulum of opinion in this direction began after the 1914–18 war, and it is now widely believed that pregnancy has less importance than the extent of the disease and the adequacy of its treatment. In this issue Dr. J. R. Edge presents the results of a survey of 462 women of child-bearing age who were admitted to the Brompton Hospital during the years 1945 and 1946, and whose course was followed until the end of 1950. Among the questions which he investigates is the time relation between the diagnosis of pulmonary tuberculosis and parturition. It is sometimes held that the disease becomes manifest sufficiently often in the early weeks after delivery to make it likely that the illness was activated by pregnancy. He shows that this activation is unlikely, for the number of women in his series diagnosed within three months of parturition is not greater than could be ascribed to chance. In examining the effect of pregnancy on pulmonary tuberculosis in his patients Dr. Edge reviewed the progress of 47 who completed 54 pregnancies and whose course was followed afterwards for periods of between one and five years. There were also 18 patients in whom 20 pregnancies were terminated surgically. Both in patients with active and inactive tuberculosis it did not seem that the course of the disease was much different whether the pregnancy was interrupted or allowed to go to term. He draws the conclusion that there is probably no indication for therapeutic abortion, and in addition he believes that the course of the disease in his series of patients was not affected by the pregnancy, whether this was terminated or allowed to continue.

Another very recent study by Cohen and his colleagues[1] follows the course over periods of between five and twenty years of 149 tuberculous mothers with 401 full-term pregnancies. These authors come to the general conclusion that neither gestation nor the first post-partum year has any deleterious influence on the course of tuberculosis. They describe the methods of treatment used in their pregnant patients, and consider that the indications and contraindications for pneumothorax, surgical collapse of the lung, and excision are the same as for non-pregnant tuberculous patients. In their view modification of treatment because of associated pregnancy is rarely necessary. However, they advise that the third trimester of pregnancy should not be disturbed by a major operation because of the danger of inducing premature delivery. They use streptomycin during pregnancy for the same indications and in the same dosage as in the non-pregnant patient: two pregnant women received 1 gramme of streptomycin daily for 45 days without damage to the child in either case.

It seems clear that with quiescent or arrested disease therapeutic abortion is not justified if the patient can be supervised. Patients with disease likely to be controlled by treatment should continue their pregnancy and be treated in the most effective way possible. In some it may be thought unlikely that the disease will be controlled even with the thorough application of modern therapy. In such circumstances, if arrangements can be made for the child to be looked after, it may be reasonable to continue the pregnancy, but the decision will often require careful judgment on the part of the patient's doctor. In any case, if the pregnancy has lasted longer than three months it is best to allow it to continue: the question of termination must be decided before the end of the first twelve weeks.

Sir Russell Brain was re-elected President of the Royal College of Physicians of London on April 7. He was first elected President of the College in 1950.

1 *Amer. Rev. Tuberc.*, 1952, **65**, 1.

REFRESHER COURSE FOR GENERAL PRACTITIONERS

TREATMENT OF GONORRHOEA

BY

T. E. OSMOND, M.B.

Late Consulting Venereologist to the Army

The treatment of acute gonococcal urethritis may be summed up briefly in the words "200,000 units of penicillin." But there is more in it than that, for it is axiomatic throughout medicine that it is just as important to treat the patient as it is to treat the disease; moreover, gonorrhoea is almost invariably contracted from another person, and it cannot be too strongly stressed that it is the duty of every medical man to do his utmost to trace the original source of infection and bring him or her to treatment. This is necessary in the interest not only of the original person infected but also of the public health; in this connexion it is to be noted that it is an offence for any person other than a registered medical practitioner to treat venereal disease.

History

The first question a doctor should ask when confronted with a case of gonorrhoea is, "From whom did you catch this?" He should try to persuade the patient to get this person to go to a doctor and be treated; with a little tact this can be accomplished in a large proportion of cases, more particularly in civil life and when the two persons concerned are known to one another.

The second question should be, "When did you catch this?" The normal incubation period of gonorrhoea is two to five days; if it is much longer than this the suspicion that it is not a gonococcal infection but a non-specific urethritis should be aroused. The circumstances of the patient should also be the subject of inquiry, so that the risk of the infection being conveyed innocently to other members of the family may be avoided. The vaginas of little girls are particularly susceptible to infection, and vulvovaginitis is often difficult to cure; in addition the disease is in many ways far more serious in females than in males, since infection easily spreads to the pelvic organs and so may cause sterility as a result of blockage of the Fallopian tubes.

Examination

For this purpose it is wise to get the patient to strip or at least expose the whole of the genital area so that the genital organs, surrounding skin, and inguinal glands can be examined, including the perianal region. If, as is usual, there is a purulent discharge it is important to be sure that this comes from within the urethra and not from behind a tight foreskin in the case of a male or from the vagina in the case of a female. The best way to take a specimen is to pick up a little pus with a previously flamed platinum loop from within the urethra after swabbing the outside with cotton-wool soaked in saline. The pus is placed on a clean slide, spread evenly by means of another slide, as in making a blood film, and allowed to dry in the air. The film should then be stained by Jensen's modification of Gram's method and examined for Gram-negative intracellular diplococci; if there is any question of legal proceedings a culture should be taken as well, by implanting some of the pus in a tube or plate containing McLeod's chocolate agar or other suitable medium, and the tube or plate should be incubated without delay. This latter procedure is necessary, as a positive culture is the only legal proof of gonorrhoea. Bacteriological examination is essential, since by no means all urethral or vaginal discharges are gonococcal in origin; in fact non-specific urethritis is nearly if not quite as common in this country as gonorrhoea in the male, and there are numerous common causes of a vaginal discharge in the female. In the latter it is well to examine the anus and rectum, because these are often involved in gonococcal infection.

It is wise to make a general as well as a local examination to exclude other conditions, particularly syphilis, and to discover if there are any complications, such as epipidymitis or salpingitis. The urine should be examined by the two-glass test. If that in the first is hazy and that in the second clear, the inflammation is largely confined to the anterior urethra. If that in both glasses is hazy the posterior urethra is probably also involved. This is a somewhat rough-and-ready test, but when posterior urethritis is present a sharp look-out should be kept for complications.

A specimen of blood for the Wassermann or similar test should be taken at the first visit, since syphilis may have been contracted at the same time as gonorrhoea; the test should be repeated from time to time over a period of at least three months.

Treatment

If after examination a firm diagnosis of acute gonococcal urethritis is made specific treatment should be applied at once. If it is not practicable to stain and examine a smear at the first session, and if the history and clinical appearances both point definitely to gonorrhoea, a dose of 150,000 to 200,000 units of penicillin may be injected. Should the diagnosis not be confirmed no harm will have been done, and if the case is one of gonorrhoea there are at least 90 chances in 100 that cure will be obtained and that the discharge will disappear in 24 hours or so. There are two good reasons for avoiding any delay: the patient will be rendered non-contagious within a matter of hours; and if he is allowed to go away pending the result of the slide examination he may not return. In the great majority of cases, both male and female, signs and symptoms disappear rapidly and no further active treatment is required. Should the condition persist as indicated by a continuance of the discharge, and especially if it still contains gonococci 24 to 48 hours after the injection of penicillin, a second dose of penicillin, double the first, should be given. Up to the present no strain of penicillin-resistant gonococcus has been met with, but some strains are more resistant than others. If a second dose does not effect cure within a few days it is almost certain that the patient either is not suffering from gonorrhoea or has a superadded infection—that is, a non-specific urethritis in addition.

Penicillin may be given in any of three forms—as the soluble sodium salt, with procaine, or with procaine and aluminium monostearate (the so-called repository preparation). The penicillin is best given parenterally, by injection into the upper and outer quadrant of the buttock, though some prefer the muscles on the outer side of the thigh. If the preparation containing aluminium is used it is important to make sure that the point of the needle does not enter a deep vein, as this may cause alarming symptoms.

It is as well, before giving any penicillin, to inquire if the patient has ever had penicillin before and if it has produced any untoward symptoms, for if the patient is penicillin-sensitive a troublesome rash or other unpleasant effects may ensue.

It is possible to effect a cure with oral penicillin, but the dose must be much larger than when it is given parenterally and the result is less certain. As alternatives to penicillin other antibiotics may be tried; the following have been found to be effective: "terramycin" by mouth, 1 g. followed six hours later by another 1 g.; "aureomycin," three 250-mg. capsules at intervals of six hours or 500 mg. followed by another 500 mg. six hours later; chloramphenicol, three capsules each of 250 mg. at equal intervals during the day; streptomycin, 750 mg. injected intramuscularly daily for three days. The last-named has the advantage that it is less likely than the others to mask a concurrent syphilis.

Risk of Masking Syphilis

The one great objection to the use of penicillin is that it may mask syphilis. The incubation period of syphilis is usually about three weeks, with extremes of 10 and 90 days, and the effect of a subcurative dose of penicillin may be to prolong this considerably or even to render the syphilis asymptomatic, with the danger of the patient developing complications of the disease, such as tabes or general paralysis of the insane, years later. For this reason some venereologists start treatment with one of the sulphonamides by mouth and only have recourse to penicillin if this fails. A suitable dosage is "sulphatriad," 5 g. a day for four days or 4 g. a day for five days; other sulphonamides may be used at the discretion of the doctor, but it is wise to choose those least likely to cause side-effects. Unfortunately so many strains of gonococci nowadays are sulphonamide-resistant that the prospect of their successful use is not very good.

Tests of Cure

Tests of cure need to be less rigorous than in the pre-penicillin era, but are still necessary, more particularly if there have been complications, and should extend over at least three months. In both sexes microscopical and cultural tests should be made from any material available—for example, discharge from urethra or cervix and threads in the urine; in the male the fluid expressed by prostato-vesicular massage should be examined, and in the female special attention should be paid to Skene's ducts, Bartholin's glands, and the cervix uteri, particularly immediately after each menstrual period. Passage of sounds and urethroscopy are needed only if stricture or folliculitis is suspected. Serum tests to exclude syphilis should be performed at least once a month, and a complement-fixation test, using a gonococcal antigen, is useful if there have been complications or if the test has previously been positive.

Complications

The space available precludes a full discussion of the complications of gonorrhoea. Many of them will require to be dealt with by a specialist who has the necessary facilities.

Most of the common and especially the acute complications react well to penicillin, but where there is a closed focus it may be necessary to take steps to establish drainage. In chronic prostatitis massage of the organ every four days is helpful; abscess of the para-urethral or Tyson's glands may require the use of the electric cautery; a peri-urethral abscess may need to be opened, preferably from within the urethra, in order to avoid the risk of a fistula; littritis is best dealt with by dilatation with a Kollmann's dilator or by cauterization through a urethroscope; cowperitis or abscess of the gland usually clears up after gentle massage with one finger in the rectum and another on the perineum; epididymitis, if resistant or causing much pain, is often relieved by the insertion into the swelling of a fairly large bore needle—open incision should be avoided.

Arthritis which does not react to penicillin should raise the suspicion that it is not gonococcal. Opinion is veering more and more to the view that chronic arthritis occurring after gonorrhoea is usually due to some other cause. Nevertheless treatment in acute cases should consist in putting the joint at rest, between sandbags if any of the joints of the leg are involved, or with light-fitting splints or a sling in the case of the elbow or wrist. Light massage and passive movements will be necessary to avoid fixation. Should the joint become unduly distended with fluid, though it never suppurates, it may be aspirated with the strictest aseptic precautions, but this is rarely necessary. Local applications such as kaolin poultices and short-wave diathermy relieve pain and promote absorption. In resistant cases some form of fever therapy is indicated: the simplest method is the intravenous injection of T.A.B. vaccine, the patient being warned that this will cause a more or less severe rigor within a few hours. A more effective form of fever treatment is to raise the patient's temperature to 105 or 106° F. (40.6 or 41.1° C.) in a Kettering hypertherm or similar apparatus, but this procedure involves some risk and should be undertaken only by a highly skilled team. It need hardly be added that, from the start, the original focus of infection, which in the male is almost invariably in the prostate and seminal vesicles, should have been dealt with by the measures already outlined.

Gonococcal ophthalmia, conjunctivitis, iritis, and irido-cyclitis usually react well to parenteral penicillin, but in the first-named unless improvement is rapid it is wise to keep the pupil dilated with atropine to prevent the formation of adhesions; in established or resistant cases pyretic treatment is indicated.

Gonococcal infection of the skin calls for no special comment. Keratodermia blennorrhagica, long supposed to be due to the gonococcus, is almost certainly caused by other organisms. Its treatment is essentially that of the original cause.

Urethral stricture is rapidly becoming a rarity but is occasionally met with in old-standing or untreated cases. Retention of urine in early acute posterior urethritis is due to spasm rather than stricture and reacts to sedative measures. An established fibrous stricture, which can be diagnosed satisfactorily only by means of the urethroscope, is treated by dilatation with progressively larger sounds or by means of Kollmann's dilator. Instrumental treatment should not be repeated more often than every four to five days, and should always be preceded and followed by cleansing of the urethra with a suitable mild antiseptic such as mercury oxycyanide 1/8,000.

When cure is delayed in women special attention should be paid to Skene's tubules, Bartholin's glands, and the cervix uteri. A common complication is salpingitis, for which operation should never, or hardly ever, be undertaken; conservative measures are usually adequate.

Conclusion

The ordinary acute case of gonorrhoea, seen and treated early, offers no difficulty. The gonococcus is perhaps the most penicillin-sensitive of all known micro-organisms and failure of cure renders it almost certain that other causes are at work. It is not uncommon for gonorrhoea and non-specific urethritis to be present at the same time; the former will clear and the latter persist under penicillin treatment, giving the impression that the gonococcus is resistant; bacteriological examination will almost certainly disprove this.

As was said at the beginning, it is important to treat the patient as well as the disease. The doctor should impress on the patient the gravity of the condition, but at the same time adopt an optimistic attitude as regards cure provided the patient carefully follows instructions. Care should be taken to explain the reasons for taking all possible steps to prevent the infection being carried to the patient's eyes or to other persons. Advice should be given on simple precautions to prevent complications, such as the avoidance of strenuous exercise, sexual intercourse, and alcohol during the acute stage.

Finally, it should be remembered that a person who contracts gonorrhoea is usually liable to expose himself to infection again. Most young men (and most gonorrhoea patients are young men) when they go to the doctor are full

of protestations that this is the "first and last time," "never again." Good intentions are apt to be ephemeral, and it is well to explain how, if exposure is repeated, the risk of infection can be reduced by careful personal hygiene immediately after the act and even more by the intelligent use of a condom.

Next Refresher Course Article.—"Medico-legal Aspects of Abortion," by Dr. Donald Teare.

THE SUPRARENAL CORTEX

[BY A SPECIAL CORRESPONDENT]

It is a truism to observe how rapidly the achievements of Kendall and Reichstein in steroid chemistry have been developed and applied. The researches initiated by their work are reaching successful conclusions. More is now known about the adrenocorticotropic hormone than any of the other anterior-pituitary hormones. Its effects on the adrenal cortex are being rapidly explored and the adrenocortical hormones secreted into human blood have now been recognized. The part played by the adrenocortical hormones in the maintenance of homoeostasis and the disturbances of equilibrium occurring in disease receive increasing attention. The possibilities and the limitations of therapy with the steroids are almost fully explored and the final surgical experiment of total adrenalectomy has many times been made. When these methods of attack are exhausted in the next few years further developments will wait upon the activities of the cytologist and his knowledge of enzyme systems.

It was at an apposite moment, then, that the Colston Research Society and the University of Bristol generously decided to invite distinguished experts in the field of the suprarenal cortex to discuss the results of their researches and their problems at a symposium of a hundred members. The director of the symposium was Professor J. M. Yoffey, and the guests and members were welcomed by Sir Philip Morris, vice-chancellor of the University of Bristol.

Two Adrenocorticotropic Hormones

The first paper, by Dr. C. H. LI, of California, showed the rapid progress made by the chemists. He concluded that the final fraction in the purification of A.C.T.H. by Astwood's valuable oxycellulose procedure was a highly potent polypeptide with a molecular weight of 10,000 and a *p*H of 9. Although the other contributors to this first session, Dr. C. J. O. R. MORRIS and Professor F. G. YOUNG, were not prepared to define the final fraction by their methods of purification so precisely as was Dr. Li, it was readily apparent that several groups of workers were travelling rapidly along converging paths. It was agreed that there might well prove to be two adrenocorticotropic hormones. Dr. Li's evidence for this depended on an inadequate correlation between the ascorbic-acid depletion test and six other assays of adrenocortical function. Professor Young, by his ion-exchange fractionation method, had also retained two different fractions. He was content with the ascorbic-acid depletion assay as a test of adrenocortical function. Dr. F. G. PRUNTY asked in another session what was the connexion between ascorbic-acid and steroid metabolism, since his scorbutic guinea-pigs maintained their adrenocortical function very nicely. His intervention suggested that such conferences as this would be improved if a selected speaker at each session reminded the members of the large areas of ignorance which the research commandos had left in the rear of their rapid advances.

To complete the story of chemical triumphs, Dr. H. HOAGLAND, of the Worcester Foundation, described the formation of the active steroids in the perfused adrenal. A.C.T.H. removed the side-chain from pregnenolone to form progesterone, and from progesterone was formed hydrocortisone (compound F) and corticosterone. Professor G. F. MARRIAN, of Edinburgh, again played the useful role of destructive critic in considering the estimation of formaldehydogenic steroids. Such chemical assays in urine were unreliable and bore no certain relation to adrenocortical function. He and his colleagues were working on the 20-methyl steroids in urine. The glucuronidase method was not yet sufficiently standardized to become a routine laboratory procedure.

Development and Functions of the Cortex

The anatomists and the physiologists continued the story. Professor YOFFEY finally discarded the oddly persistent idea that the three layers of the adrenal cortex developed from without inwards. The active region was the zona reticularis and the most active area was an intermediate zone between this layer and the zona fasciculata. Professor F. VERZAR, of Basle, designated the cell as the site of adrenocortical action. Here the corticosteroids manipulated a metabolic switchboard so that glucose was converted to glycogen, glucose to fat, and protein to glycogen. Glycogen catabolism was inhibited under all conditions, and linked with these alterations in carbohydrate metabolism was the action on electrolytes, for potassium accompanied glycogen into the cell and glucose was an essential element in the sodium-potassium exchange. These metabolic changes were achieved through the enzyme systems. Dr. MARTHE VOGT, of Edinburgh, described with great clarity the influence of the hypothalamus, the adrenal medulla, and the level of A.C.T.H. on adrenocorticotropic secretion. Despite the hypophyseal transplant experiments, control appeared to lie in the hypothalamus.

Total Adrenalectomy in Mental Disorders

Precise knowledge of the nature and mechanism of the hypothalamic control of individual anterior-pituitary hormones is essential for a picture of the relationship between the psyche and the endocrine and autonomic nervous systems, but understanding of this central co-ordination lags behind our knowledge of the peripheral mechanisms. Nevertheless, a few psychiatrists like Drs. M. REISS and R. E. HEMPHILL, of Bristol, have emphasized the importance of endocrine changes in the psychoses. They outlined again their evidence for adrenocortical dysfunction in mental disorders. Dr. HOAGLAND supported this view with further figures, but surprised the symposium with the information that these results had been considered to justify therapeutic total bilateral adrenalectomy. This operation had now been performed on six schizophrenic patients who were being maintained in good physical health by substitution therapy. An opportunity had thus been given for the performance of perfusion experiments on the removed human adrenal. Dr. A. SEGALOFF, of New Orleans, was perturbed that such treatment should be based on a disturbance of adrenocortical function which was plainly not primary. Dr. D. J. INGLE, of Michigan, when discussing Selye's hypothesis of the diseases of adaptation, also emphasized that adrenocortical dysfunction was rarely a primary agent in disease.

Limitations of Chemistry

Professor S. ZUCKERMAN protested against the action of the chemists, who were fractionating and disarticulating proteins until all physiological reality had disappeared from their fractions. The chemist must acknowledge that the final criteria were biological and that the interplay of the anterior pituitary, the adrenal cortex, and the gonads represented a complicated pattern which was capable of kaleidoscopic adjustment. Professor YOUNG was robustly unrepentant. This chemical characterization must proceed, and when it was complete the biologists would have a scientific basis for their homoeostatic patterns. Although Professor Young had the better of the argument, it was right that Professor Zuckerman should insist on the satisfaction of biological criteria as the ultimate test of biochemical research, and right also that such lively and fundamental debate should proceed in the friendly surroundings provided by the Colston Research Society at Bristol.

Correspondence

Because of the present high cost of producing the Journal, and the great pressure on our space, correspondents are asked to keep their letters short.

Prolonged Respiratory Paralysis after Succinylcholine

SIR,—The following case is, I feel, worthy of publication. A healthy man aged 33 and weighing approximately 12½ st. (79.4 kg.), with a blood pressure of 150/90, required the removal of a calcaneal spur. The prone position was necessary.

The anaesthetic procedure was 0.7 g. thiopentone followed by 80 mg. "scoline" (succinylcholine chloride) intravenously. The usual muscular twitchings occurred, but these were not more marked than normal. He was inflated with oxygen and an oro-tracheal tube was inserted with ease. Respiration did not begin spontaneously in the usual three to five minutes and inflation was carried out manually with a 50% O_2:N_2O mixture. The operation was completed satisfactorily. At the end of 45 minutes, however, respiratory paralysis was still present, the condition of the patient was excellent—i.e., colour good, pupils pinpoint (due to premedication with ¼ gr. (22 mg.) "omnopon"), eyeballs moist, pulse rate 60 per minute: the blood pressure did, however, show a rise to 190/100 due unquestionably to a CO_2 "pile up," although an adequate flow rate of gases was maintained.

Attempts at stimulation of his respiratory centre were now made—nikethamide and lobeline were given intravenously with no effect. Although it was realized that "prostigmin" would probably prolong the scoline effect, it was given with atropine intravenously. No change in the condition was apparent.

As the patient was in good condition, I put him in a respirator, leaving him connected to the anaesthetic machine and using a high flow rate of oxygen only. It was found, however, that his colour was not quite so well maintained by the respirator as when manual compression of the rebreathing bag was performed. No check on his blood pressure was possible at this time, but his pulse rate remained steady at 60 and his general condition was unchanged. The outcome was satisfactory—three hours after the scoline administration he began to strain on the oro-tracheal tube, and weak diaphragmatic respiratory movements began. The oro-tracheal tube was replaced by a Phillips airway. He was taken out of the respirator, and his respirations were aided; half an hour later his respirations were normal and he recovered consciousness. His blood pressure was now 110/70, reflexes normal, and his general condition was perfect. He had no memory of the event and was soon sitting up and smoking. He was observed carefully for a few days following this mishap and showed no abnormality of any kind.

It is worth noting that scoline occasionally can produce a prolonged effect: the reason for this is obscure, but it might conceivably be due to some alteration of the patient's *p*H to the acid side, thus slowing up the breakdown of the drug. Whether an alkaline infusion would hasten recovery merits investigation. As expected, respiratory stimulants are useless. Prostigmin undoubtedly prolongs the paralysant effect, as other cases of this sort in which it had not been used recovered in about two hours.

The use of a respirator for a respiratory paralysis following the administration of a relaxant is noteworthy.

It is unusual to find the effect of a relatively small dose of thiopentone persisting for three hours, as suggested by the patient having no memory of the event: can there be a synergistic effect?

The use of scoline for abdominal closure can be more troublesome than the administration of a few ml. thiopentone, and in electro-convulsion therapy decamethonium or gallamine triethiodide might be the drugs of choice rather than scoline, as I have seen no similar mishaps when using these.—I am, etc.,

London, W.1. J. KENNEDY HARPER.

Dangers of Enemata in Megacolon

SIR,—The report by Mr. A. Jolleys (March 29, p. 692) of death in a child with Hirschsprung's disease is a salutary lesson on the dangers of what many regard as a harmless diagnostic procedure. Such tragedies may well be commoner than is generally acknowledged. I remember a very similar case of a boy aged 4, with Hirschsprung's disease, who was also given about four pints (2 l.) of fluids per rectum (in the form of a barium and subsequent clearing enemas). In this instance, too, the fluid was rapidly absorbed and followed by pallor, sweating, vomiting, convulsions, and death; heavy sedation and venesection were of no avail. It seems probable, as suggested by Mr. Jolleys, that the cause of death was water intoxication.

It is very questionable whether it is ever necessary for such large quantities of fluids to be given rectally to children. The requisite information can be obtained by the use of only a small amount of barium (Swenson *et al.*, *Pediatrics*, 1949, **4**, 201). Briefly, the patient is screened in an oblique position, when the narrow rectum and rectosigmoid distal to the markedly dilated sigmoid can be observed. These important changes in the rectum and rectosigmoid are missed if the lower colon is "ballooned out" with large amounts of barium. The routine adoption of this technique would obviate the two main complications following large barium enemas—the precipitation of intestinal obstruction and water intoxication.—I am, etc.,

Halifax. W. P. SWEETNAM.

Family Planning

SIR,—It has been my privilege to study 1,000 signed letters, taken at random from the vast correspondence amassed by Professor David Mace, consequent upon his Tuesday evening articles in the *Star*. Despite the fact that his articles do not deal directly with sex matters, 296 of this group of Professor Mace's correspondents sought information relating to one or more aspects of sex. Among these:

69 asked for advice on reliable sex literature.

25 were worried about personal matters. For example, there was fear that marriage would not be ethical, due to hysterectomy in three cases, a belief that the penis was undersized in two cases, and hypospadias in one case.

17 wanted to be sure of correct teaching of the facts of life either for themselves or for their children.

44 wished to obtain premarital instruction about sex relations in marriage.

99 sought aid with their marital sex adjustment (other than contraception). Some of them complained of the unhelpful attitude adopted by their doctor. About half experienced maladjustment at the beginning of their marriage, and half after a normal sex relationship had once been established. Many cases arose after the birth of children or following war separation, and 11 at about the time of the climacteric. As a result of their sexual difficulties, 18 felt they were narrowly missing an almost perfect relationship, 37 were very unhappy, and 30 feared marital breakdown.

61 asked for sound teaching about contraceptive methods, or from whom this might be obtained. Their letters clearly demonstrate the chaos and urgent need for reform in this field, and provide a sad record of tormenting worry, repeated failures of contraception resulting from ignorance, resort to criminal abortion or to undesired celibacy within marriage, and the strains on the marital relationship such evils involve.

40 longed for children. 25 of them asked to be referred to a fertility clinic or second medical opinion (11 had already been under their doctor). Most of the rest wished to adopt a child.

16 asked eugenic questions (10 with regard to cousin marriage).

Other facts which emerged were:

(*a*) Even to-day individuals of adult age may lack elementary knowledge of sex.

(*b*) Sheer embarrassment prevents some people from either consulting their doctor or attending a clinic about intimate matters.

(*c*) Engaged persons may desire premarital medical overhaul, yet not know how to obtain it in cases where their own doctor is unable to help them.

(*d*) The small but perceptible demand for voluntary sterilization is related to unsatisfactory contraception.

(*e*) Professional advice alleged to have been given to a sexually frustrated husband to seek his pleasures elsewhere was unacceptable to the patient and the reason for his writing to a lay authority.

The bulk of the remaining letters were about non-medical aspects of marriage difficulty, but constant reference was made in them to morbid symptoms following marital disharmony. Some of the sufferers were worried by the deterioration in the quality of their work, and others felt impelled to visit their doctor. Evidence in this correspondence seems to indicate that:

(1) The recommendations passed by the council of the Medical Women's Federation should be implemented as soon as possible (*British Medical Journal*, March 15, p. 597).

(2) At least one doctor of each sex, of suitable personality and training (preferably married), should be available in every district for consultation by those with marital sex maladjustment. Such doctors should also be willing to undertake premarital medical examination, and thus become more easily approached by those who have had the advantage of such examination if some difficulty which could not be entirely avoided should arise after marriage.

(3) Couples severely worried by their childlessness should know that they have the opportunity of a full investigation if they so wish, unless a definite contraindication is known to their doctor. In that case the position should be carefully explained and the patients led to realize that everything humanly possible has been done in their case.

(4) There should be public display of a list of reliable books (such as has been prepared by the Marriage Guidance Council), with an annotation on the subjects dealt with in each book, its price, and where it may be obtained. These lists should appear in all public clinics, the waiting-rooms of doctors willing to co-operate, booksellers, and perhaps chemists' shops. It is desirable that there should also be a local centre for the loan of these books (possibly the public library), as cost is a known deterrent to their more general use.

(5) The campaign by responsible people in the popular press should continue, since there is considerable evidence that newspaper articles reach otherwise inaccessible people, and contact made through letters can reassure correspondents and guide them to seek help in person from their own doctor or other suitable source.

I wish to thank Professor Mace for permission to use this material, but he should not be held responsible for any of the views expressed.—I am, etc.,

Harrow. JOAN HOUSEMAN.

SIR,—Dr. Letitia Fairfield (March 29, p. 708) is right in stating that there is considerable danger in the trend towards universal effective family planning; this trend would be speeded by a comprehensive contraceptive service. The trend is creating a major change in the environment, a change to which much of our population is genetically and socially ill-adapted. The extent of our present failure to have sufficient children for population replacement would be much increased if there were no children born above the number planned by parents, and we do not know for certain if a population planning the size of its families would ever be capable of maintaining itself.

But, though risky, a comprehensive contraceptive service would not necessarily be disastrous. Self-applied selection is likely to provide in time an automatic check to a population fall. Men and women are likely on the whole, for both genetic and environmental reasons, to copy their parents in the size of the family they plan. Those groups and families who are not prepared to face prolonged hardship or are afraid of bringing up children to be cannon-fodder are likely to plan families of two children or less, and so eliminate themselves; in each generation an increasing proportion of the population will be derived from groups and families who are both fond of children and sufficiently tough-minded to face hardships not only for themselves but for their children.

It is probably better for the medical profession not to attempt to delay this evolutionary process by denying access to contraception to those who want only two children or less. They should perhaps advise the ordinary fit young couple to have three or four children before they are 30 and they should set an example themselves; but newly married couples should be given the information and means, appropriate to their religious belief, to choose for themselves whether they take this advice or not.—I am, etc.,

Orpington, Kent. C. O. CARTER.

SIR,—Is it really necessary to have yet more clinics—at public expense—with the inevitable hordes of specialists, technicians, nurses, and clerks and filing cabinets? Why should it be necessary to have a clinic attached to a maternity hospital or maternity home to teach the technique of avoiding pregnancy? Horrible thought! Surely with such excellent facilities for antenatal care, vitamins, and extra rations, expert attention and accommodation for the confinement, and many provisions and allowances for the growing children and their education, there should now be less need than ever for the restriction of families.

Who exactly are these women for whom it is recommended to provide free contraceptive clinics under the National Health Scheme? Why should these be provided with official or national encouragement to instruct in methods of contraception, or, more euphemistically, family planning (planning, planning), or family spacing, or family avoidance?

The "Memorandum on Family Planning" (*Journal*, March 15, p. 595) tells us these "fall into two main groups. First, those who on medical grounds have been advised to avoid pregnancy." For this comparatively small group one would think that the experts who give such advice would have ample opportunity at the consultation when voicing such an opinion, or during the antenatal care, during the puerperium, or at the postnatal examination, of advising how pregnancy could be avoided or directing to some private person or clinic where instruction could be given. It is very important, however, that such a grave opinion, often, I fear, glibly voiced for inadequate reasons, should be most carefully considered. During more than thirty years of family practice in which obstetrics was my chief interest, I have been surprised at the number of women, nulliparous and multiparous, to whom this alarming advice had been given for no reason which could be discovered. After years of disappointment and worry, many of them had perfectly normal pregnancies and confinements.

"The second and continually expanding group is made up of women who wish to plan their family with intervals between the births of their children." Who are these women? And what is their economic status? The anaemic, weakly, over-tired woman with a number of children would receive any necessary advice, free, on medical grounds, and presumably most of these are under the eye of the public health department and health visitors. Probably the feckless, illiterate type who produce large families in squalor would continue to do so even if a clinic was placed in every street. They either would not bother to make use of the services offered or would be too careless or inept in carrying out instructions. In my experience a large proportion of those most concerned about contraception are physically fit and reasonably well endowed financially to accept the responsibilities of parenthood. Many of those who talk of family spacing terminate the family after the birth of the second child. This is more probable if they have "one of each sort"; if not, there may be a third. We all know the arguments for the delay of the family—housing difficulties, and the desire to be firmly established and luxuriously furnished, including car and television set, before having any children. This may be plausible enough in some cases, but ought we to spend large sums of money on these persons to teach them to realize their schemes of family avoidance or spacing, which in after years they may bitterly regret?

The idea that clinics should be provided to obviate criminal abortion may not be wholly sound. Other planners might hear of this—the house planners, for example—and require that all houses be fitted with outside ladders—as fire escapes, of course—so that cat burglars would have less risk of personal injury.

I am pleased to note the warning in Dr. Fairfield's letter (March 29, p. 708), but is it not time we created an atmosphere or climate of opinion in favour of larger families among those who are strong and healthy and in a satisfactory financial position, and so give the children the chance of the finest possible upbringing, that of affectionate rivalry and unselfishness best engendered in the larger family?

The distress of the pregnant woman is not always due to fear for her own health or of any imagined difficulty in caring for the unborn child, financial or otherwise. Frequently it is due to the thought of what her neighbours, friends, or relatives will think of her for-"having another one." I remember one such patient greatly perturbed and apprehensive and "ashamed," she said, but she feared only the comment of her own mother. I also met a gentleman so distressed at the "dressing down" of his father-in-law, not his wife, that he settled the question of restricting his family by slashing off his scrotum and testicles and disposing of them in the bathroom.

We must all agree that there may be justification for contraception in the case of certain individuals or certain

groups, and for a variety of reasons; whether it be achieved by the aesthetic methods of the Catholics, or whether the less considerate husband necessitates artificial devices and the vast organization under discussion, are we not fostering this very dangerous idea far too enthusiastically and too comprehensively?

I am inclined to think, though it may be courageous, that the recommendation of the learned council of the Medical Women's Federation is like the curate's egg, perhaps worse.—I am, etc.,

Huddersfield. S. H. WADDY.

SIR,—I feel strongly that one of the points raised in Dr. Letitia Fairfield's letter (March 29, p. 708) is much worth going into—that of the vexed question of the giving of contraceptive advice. Along with a general feeling of approval of the findings of the Medical Women's Federation report, I find that there is one aspect of the picture which should be examined carefully.

Had our own profession not failed in making contraceptive advice on medical grounds readily available in the past the main driving factor in establishing the Family Planning Association would not have existed. Its existence, though excellent work has doubtless been done, is a constant reminder of our neglect, which should be dealt with. As the report states (March 15, p. 595) professional advice on this subject (where the religious beliefs allow of it) should be given as part of the Health Service. Already established centres such as the antenatal clinics could perhaps give one session in every 10 (more or less frequently according to local need) for this purpose. At these sessions, cases referred by practitioners or social workers *on medical grounds* would be dealt with, as also could the cases of sexual difficulties, on which stress has recently been laid, which are known to be too time-consuming for the routine surgery hour.

It is argued that such advice is only one aspect of the work dealt with by this association. Surely the others could also be adequately coped with by institutions already in existence. The financial factor which at one time prevented many women from asking their own doctor's advice on minor gynaecological problems now no longer exists. Sterility problems are most efficiently dealt with at a sterility clinic. Marriage guidance in its social aspect could be dealt with by trained social workers.

In querying the wisdom of advice on "family spacing," however, Dr. Fairfield really touches on the heart of the matter. Nothing is surer than that the "spacing" is liable to develop from limitation to, in many cases, a complete full-stop in the growth of the family.

If Britain is to survive at all surely she must stimulate all methods of encouraging an increase in the birth rate. And as surely it is our duty as doctors to encourage any constructive attitude in the matter rather than support destructive tendencies. Let us have a Family Planning Association by all means—but let it be an association whose avowed aim is to *help mothers overcome the social factors which tend to make them wish to limit their families*. These factors have already been scientifically assessed. The larger ones, such as housing, cost of living, etc., are governed by national and international factors outside our personal influence except through the very frail medium of our voting power. The smaller social factors are *not uncontrollable*. Surely the constant tie and endless hard work in bringing up a large young family are almost as potent deterrents as are those bigger factors.

If the voluntary helpers who enter with such enthusiasm into the present family planning campaign would harness their energy to partly alleviating this by providing, say, crèche facilities in these areas (even if only for two days every month) how much more productive an occupation it would be than handing out contraceptive appliances and keeping notes of their sale.

Or if they could organize a day's household helping or mending to assist such a mother and relieve her of the overtiredness which makes her bicker with her husband, how much more sensible than carrying out deep-laid investigations into why her marriage looks like going on the rocks.

What a sadly decadent state of affairs we are complacently fostering in our native land. On one end of the scale the manufacture of arms to destroy life, and at the other end medically assisted guidance on how to prevent new life from ever even starting.

—I am, etc.,

Berwick-on-Tweed. AGNES R. S. SADLER.

SIR,—The Subcommittee of the Medical Women's Federation has drawn attention to the need for teaching birth-control methods to students. Wise teaching is needed, not only of the techniques but to discuss the social and marriage relationship problems with which general practitioners are bound to meet. Instruction in birth control should be more than fitting the patient and teaching a manœuvre. A birth-control consultation should begin by a discussion with the patient of the pros and cons and limitations of the various methods, the known and unknown factors of fertility in each married couple, and other comments on the social and family aspects of contraception. Where possible this discussion should be with both husband and wife, and in any case the woman should have an opportunity of discussing with her husband the various points raised by the doctor, many of which will be quite new to both of them.

The family doctor is usually the most suitable doctor to give this advice, but clinics will be needed in many places. The ease and cheapness and efficiency of the sheath and the fact that there is no attempt to deceive the other party make it important to view the drive to extend women's contraceptive equipment critically. I do not think contraceptive advice should ever be free unless the case is assessed as being in need of help. The fact that advice is obtainable may be freely advertised by word of mouth or posters, but seeking the advice should be a deliberate responsible move by the patient. Personally I never instruct a Catholic patient in the use of mechanical methods, but with the husband's consent and after advising them to consult their priest I teach the theory of the safe period with the help of the daily morning temperature chart. My view is that it is not a doctor's job to urge or help a patient to act against her religion or to give her cause for guilty feelings.

A doctor undertaking to give birth-control advice is undertaking a serious responsibility. The relationship of man and wife and family is a complex affair. A woman fearful of conceiving may need other help than freely accessible birth control. A husband may need to be reassured that to employ birth control is not physically harmful. Who knows where happiness lies? "Our art is great and the mind of man presses ever forward."—I am, etc.,

London, N.2. JEAN LAURIE.

Isonicotinic Hydrazide as Wonder Drug

SIR,—The two most astonishing things about this "wonder drug" are, first, that no one from England seems to have been sent out to investigate, and, secondly, that the English medical press had not got the American information. I was much more fortunate, for I knew of the work, and on March 5, at the Altein Sanatorium in Arosa, Dr. Tanner, the director, afforded me the privilege of looking at the cases treated with "rimifon," and also seeing their dossiers, and in addition the American literature, which was all there in type. The following few days some 350 doctors of Europe and the Near East had gathered at Arosa for a conference, and among other things to get a report from Dr. Tanner.

This report, as a result of a conference with Professor Eerland and myself, Dr. Tanner made very, very brief, and he stated that it was the agreed opinion of Eerland, Tanner, and myself that "to-day there cannot be said anything with certainty about rimifon." He indicated that some patients had put on weight, some had not. Sedimentations had improved in some and not in others. None had converted the sputum, though there was a diminution of the bacilli in some. Cough improved in many, became worse in others. Most important, he stated, "Yesterday a patient suffering from caseous tuberculosis died, in spite of rimifon." He pointed out that constipation and vertigo were the principal general appearances, but no serious complication had been observed. He indicated that the psychological reaction had to be taken into account, and further that to-day we did not know the right dose, we knew nothing of the reaction of the bacillus under the treatment, and we did not know if resistance was to be feared. He wisely stated, "I do not believe that we have the right to leave the approved therapeutic remedies and the approved indications." From my experience of those patients I agree with what Dr. Tanner

said on March 5, that the drug does something and it may lead to something better.

It is sad, but easily understood, that the drug firms are now producing this medicament under various names. Some of us had already started a controlled experiment before the publicity. To date I agree with Dr. Tanner that it is too early to give any information, except that patients should not have false hopes raised and that doctors in general should not prescribe it until the results of controlled experiments are known.—I am, etc.,

Market Drayton, Salop. PETER W. EDWARDS.

Congestive and Simple Glaucoma

SIR,—May I submit that the word "simple," as applied to glaucoma, should be dropped (see *Journal*, March 29, p. 712)? It is too vague, and there are other well-established terms which are more descriptive. Primary glaucoma occurs in two main forms—namely, congestive and non-congestive. The congestive kind is generally *acute*, and the non-congestive generally *chronic*. There is also an intermediate variety, mildly congestive and generally *subacute*.

I think that the recognized classification into acute, subacute, and chronic groups covers the ground satisfactorily; and it has the merit of indicating differences which are important in practice.—I am, etc.,

Birmingham. D. PRIESTLEY SMITH.

SIR,—Mr. R. Affleck Greeves's appreciation (April 5, p. 764) of Mr. S. J. H. Miller's study of glaucoma symptoms needs no endorsement from me; but I hope that Mr. Miller's plea for more widespread vigilance towards the disease in its early stages will not pass unanswered because of Mr. Greeves's later criticism. The detection of significant changes in the central fields before the disk can be said to be pathologically cupped is, in my experience also, the first conclusive evidence of "simple" glaucoma in a small but definite group of cases. The problem of early changes in such cases is, in my opinion, a part of the more general one of the (visual) signs of lesions of the optic nerves and chiasma in which, I venture to suggest, the evidence of perimetry and scotometry is commonly of greater value in assessing the presence and extent of early changes than an opinion based upon ophthalmoscopy alone. Would Mr. Greeves not agree that the finding of characteristic field changes in these circumstances tends to diminish rather than increase the risks of misdiagnosis?—I am, etc.,

London, W.1. H. E. HOBBS.

Medical Aspects of Tobacco Smoking

SIR,—Dr. R. Bodley Scott (March 29, p. 671) appears to be in doubt about the fundamental nature of tobacco smoking. I agree with his view, thrice affirmed, that it is a drug addiction, but he also refers to it six times as a habit. Now every day-to-day activity comes within the *O.E.D.* definition of a habit, "A settled tendency or practice": even murder might, I suppose, become habitual! Nevertheless I think it wrong to refer to a drug addiction as a habit. The habit factor is purely incidental (as it would be in habitual murder!).

The sentence, "*The moralist* (italics mine) will find matter for reflection in the thought that over one-quarter of the country's income is now derived from the addiction of its inhabitants to tobacco and alcohol," implies that tobacco smoking is a moral issue—a vice. The urge to procure his drug and the drug's effects often result in actions or omissions by addicts which do not conform to the moral code of non-addicts. Clearly, however, moral degeneracy is secondary to drug-taking. It is a symptom: the disease is drug addiction.

It is surely indisputable that the drug addictions, including nicotinism and alcoholism, are specific diseases. They are specific, intermittent intoxications, each with its aetiology, symptomatology, pathology and psychopathology, and treatment. Because of their frequency, and the toxicity of tobacco smoke and of alcohol, they are probably, moreover, the most important diseases in this country. Yet they are readily preventable and curable. We virtually prevent addiction to opium and heroin, stronger drugs, but we evade our duty in respect of tobacco and alcohol. We have allowed addiction to these drugs to reach such vast proportions, indeed, that our evasion constitutes surely the greatest breach of faith in the history of medicine.

Its cause is not far to seek: a high proportion of our profession is addicted to tobacco or alcohol, or to both, and our evasion of duty is evidence of our moral degeneracy, which is symptomatic of our addiction. Whilst this may explain, nothing can excuse, our perfidy.—I am, etc.,

Wallasey. LENNOX JOHNSTON.

SIR,—I was extremely interested to read the article by Dr. R. Bodley Scott (March 29, p. 671). I disagree with him when he says that "asthma, due to tobacco, must be rare." From personal experience, I have found that certain brands, especially those used for pipe-smoking, tend to bring on attacks of asthma.

I have suffered from bronchitis almost all my life, but was lucky enough to be born into a family of non-smokers. About 20 years ago I acted as an "illness" locum for three months at a sanatorium situated in delightful country 600 ft. above sea level. It was then that I started having nightly attacks of asthma. My chief blamed everything except his own "stinking" pipe. About nine months later, when I was taking a university course, my attacks returned, causing a great many missed lectures, including the degree examination, in spite of my repeated unsuccessful requests to my colleagues to refrain from smoking.

As a chest physician, I have met numerous patients who, like myself, are convinced that tobacco smoke provokes attacks of asthma.—I am, etc.,

Leeds. DAVID A. HERD.

SIR,—With reference to the relationship between cigarette-smoking and bronchial carcinoma described by Dr. R. Bodley Scott (March 29, p. 671), and particularly the 15-fold increase in that disease between 1922 and 1947, there seems to be one discrepancy.

The steep rise in bronchial carcinoma, we are told, started in 1922, but over-indulgence in cigarette-smoking existed long before that date.

May I suggest another substance of known carcinogenic power, exposure to which fits in exactly with the dates of the rise in this disease? I refer to the paraffins in automobile exhausts. Our city streets and main roads had their atmosphere steadily contaminated by exhaust gases as the motor-car increased in numbers from the early 1920s, until the diesel engine arrived in the early 1930s to add its disgusting quota of half-burnt crude oil to the air.

It should be possible to check this suspicion, since those who live in cities and along main roads breathe air which is far more heavily contaminated than those who live elsewhere.—I am, etc.,

Droitwich. E. SHIRLEY JONES.

Value of Histamine Skin Test in Ménière's Disease

SIR,—I send this belated comment lest a test which has proved in many hands of great value should perhaps be cast aside because of adverse criticism based upon a misunderstanding of its purpose and function.

The histamine skin test does not profess to make a diagnosis, whether of Ménière's disease or allergy or of anything else. It claims only to divide patients with Ménière's syndrome, already diagnosed, into groups. Wherefore controls consisting of subjects with other diseases or no disease, of which so much is made in Dr. M. Haggie's article (1951, 2, 1057), are not in fact controls at all and have no bearing on the point at issue. However, Dr. Haggie does confirm the claim made for grouping, for in his series of Ménière cases he obtained almost precisely the same proportion of "positives" as I have in any published series. This fact was apparently obscured for him, since he makes no comment on it, by the finding of an identical proportion of "positives" in his controls. Regrettably, instead of asking himself why and continuing his investigation, he fell back on statistics and contented himself with saying, "So there."

As to the value of the test, that depends upon its efficacy as a guide to treatment, and this evaluation the author has not attempted, despite the title of his article. His has been an academic exercise. Had he proceeded to test the practical issue as others have done, along lines which I have described elsewhere (*N.Y. St. J. Med.*, 1944, **44**, 489; *Arch. Otolaryng., Chicago*, 1949, **49**, 151; ibid., 1949, **50**, 564; ibid., 1950, **51**, 149), I venture to think that he might have finished among those who, coming to scoff, remained to pray.—I am, etc.,

New York MILES ATKINSON.

Mr. Bevan

SIR,—May I be allowed to comment on your leading article (April 5, p. 749) on "Bevan's Book"? Having read Mr. Bevan's book I can only regard your leader as being an undignified, misleading, and unjust personal attack on Mr. Bevan, unworthy of publication in a professional and scientific journal such as the *British Medical Journal*.

It is unworthy in its failure to comment objectively and without bias on Mr. Bevan's chapter on the National Health Service. It is misleading in its quotation of extracts out of their context; for example, your extract about "the innumerable harpies who battened on the sick" quoted in support of your accusation that Mr. Bevan besmirches those who looked after the sick before 1948. When read in its context this clearly refers to the quacks and purveyors of patent medicines and cures and not, as you represent, to the medical profession. It is unjust in its failure to draw attention to Mr. Bevan's account of his negotiations with the B.M.A., to his statement, for example, that he "suggested a graduated system of capitation payments which would be highest in the medium ranges and lower in the higher." It is undignified in its whole tenor and tone and above all in its terminal childish attempt to prove Mr. Bevan's political adolescence.

The N.H.S. patients and doctors have too long been bedevilled by the incompatibility of the B.M.A. and Mr. Bevan, and articles like this can surely do nothing but harm. I am sure I am voicing the sentiments of a great many younger practitioners when I say that, though deeply conscious of our indebtedness to the efforts of the General Medical Services Committee of the B.M.A. for their successful and prolonged efforts on our behalf, we have the uneasy feeling that wiser direction of the early stages of our entrance into the N.H.S. would have avoided much of the difficulty and delay.

In conclusion, may I say I am not a supporter of either Mr. Bevan or the Labour Party. I am local secretary of the B.M.A., but articles of the spirit and quality of this leading article almost shame me into resignation.—I am, etc.,

Cornwall ERIC TOWNSEND.

Rh in Practice

SIR,—In your issue of March 22 (p. 667) you drew attention to the recent publication of the Medical Research Council's Memorandum No. 27, *The Rh Blood Groups and their Clinical Effects*, which is a revision of the earlier Memorandum No. 19. You described the changes as very minor and as consisting chiefly of bringing the memorandum up to date with recent references. I feel that by this statement you may inadvertently have misled some of your readers. It is true that much of the text, particularly that of the section on Rh groups, is unchanged, but important alterations have been made in the sections on clinical considerations and on Rh testing.

In the clinical section we should like to draw special attention to two main changes, the results of recent controlled trials. Premature induction of labour is stated to be inadvisable as a routine treatment for women whose serum contains anti-Rh, and exchange rather than simple transfusion is now recommended without reservation as the treatment of choice for affected infants.

In the section on Rh testing numerous changes have been made as the result of the experience of the past four or five years. The very important pages on direct matching tests have been rewritten, as have most of those on the trypsin test and on the preparation of anti-human-globulin serum.

Although these and other changes affect only a small number of pages, I think you will agree that they are of considerable practical importance.—I am, etc.,

Medical Research Council, S.W.1. SHEILA SMITH, Publications Officer.

Explosion During Anaesthetic

SIR,—I have read with interest the account in your Medico-Legal column (January 19, p. 168) of an explosion during anaesthesia.

Your correspondent states that the agents used in this case were "flaxedil," thiopentone, and oxygen. I feel that the occurrence of an explosion, as opposed to a fire, under these circumstances requires some explanation, as none of the agents used is explosive. Oxygen supports combustion but will not explode. One is therefore led to surmise that some explosive agent such as ether or cyclopropane must have found entry into the machine and that the resulting mixture was ignited by a static spark. I have personal knowledge of one such explosion which could be explained only by the fact that a trace of explosive gas had remained in the anaesthesia machine from a previous case. There may be pockets of cyclopropane or of ether vapour lying within the corrugations of the rubber hose. To my mind this is the only explanation of this occurrence—namely, that some traces of an explosive agent were still somewhere in the anaesthetic machine from a previous case.

Two points of interest emerge from the report of this mishap. First, one would be well advised when using an anaesthetic machine for supplementation with oxygen to "wash out" the tubing and breathing bag of the machine by means of a large flow of oxygen before applying the mask to the patient's face; or else to use a separate oxygen unit for this purpose. Secondly, it probably is never advisable to proceed with the operation after an explosion has occurred, however apparently satisfactory the patient's condition may be at the moment.—I am, etc.,

University of Illinois, Chicago. GORDON M. WYANT.

POINTS FROM LETTERS

Hyperplesis and Hyperplesia

Dr. D. M. CAMERON (Bristol) writes: At the risk of being called pedantic, may I plead for a return to hyperpiesia for sustained high blood pressure and hyperpiesis for a raised blood pressure? If I remember right, the original work on blood pressure was carried out by Sir Clifford Allbutt. He gave us these names. They satisfied us for many years, and I cannot understand why in the last five years or so the hybrid word has displaced the original, and now finds favour even in editorials. Since we owe to Sir Clifford the clinical thermometer we daily use, why discard the name he gave the disease? Or if the moderns find the extra syllables tiresome, and every little sign or syndrome seems to be appropriated nowadays, might we call it Allbutt's disease?

Sulphamerazine Still Dangerous

Dr. R. S. SAXTON (Brighton) writes: I am glad to see that the campaign against sulphamerazine has been revived. In my opinion the use of this drug, for which there are many adequate substitutes, should be prohibited. . . . A nurse had tonsillitis, and received only six tablets (3 g.) of sulphamerazine in 12 hours, during which she had had an alkaline mixture and a high fluid intake under the watchful eye of the home sister. The patient developed complete anuria, which was subsequently relieved by ureteric catheterization. . . . Another patient had been given the recommended doses of "cremomerazine" as a prophylactic against complications of measles, which she had. She developed anuria.

Correction

In the paper, "Daraprim (B.W. 50-63)—a new Antimalarial," by L. G. Goodwin (April 5, p. 732), the heading of Table II states the dosage to be "twice daily." This should, of course, read "twice *weekly*."

Obituary

Dr. R. W. DODGSON, a relative of "Lewis Carroll" (the Rev. C. L. Dodgson), died on March 4 at his home in Conway, Caernarvonshire. He will be remembered for his work on the transmission of typhoid fever by shellfish. Robert William Dodgson was born at Wigton, in Cumberland, in 1871, and was educated at Owens College, Manchester, and at St. Mary's Hospital, London, qualifying M.R.C.S., L.R.C.P. in 1895. In the following year he took the M.B. of the University of London, proceeding M.D. (gold medal) in 1898. He was appointed assistant pathologist at St. Mary's Hospital, and in 1899 he went to South Africa as a special service medical officer to investigate the results of anti-typhoid inoculation among British troops. From 1901 to 1903 he acted as director of the Government research laboratory at Capetown. Shortly after his return to this country he became a member of the Royal College of Physicians. In 1912 he was a member of the late Sir Almroth Wright's team which went to Johannesburg to investigate the large death rate from pneumonia among the native workers employed in the gold mines. In 1915 Dr. Dodgson was appointed bacteriologist at the Ministry of Agriculture and Fisheries research station at Conway, where he spent the rest of his career. In the previous year he reached England from Germany just four days before war was declared, having visited various laboratories on the Continent to compare the methods used there with our own. He was promoted to principal naturalist in 1921, and served as director of the fisheries research station at Conway from 1931 to 1937, being appointed consultant for shellfish services. He retired in 1939. It was at Conway that he carried out his research into the transmission of typhoid fever by shellfish. He installed large tanks in which mussels were first laid in chlorinated sea-water and then washed in fresh water. Then, free from all pollution, they were sent in sealed bags to the fishmongers. He wrote a pamphlet entitled, *Shellfish and the Public Health*, and in 1929 the Stationery Office published his report on mussel purification. His work was recognized by his appointment as O.B.E. in 1936.

The sudden death on March 5 of Dr. DAVID HUNTER DOW YOUNG at his home in Bury, Lancashire, has removed from the community a general practitioner of the best traditions. Graduating M.B., Ch.B. from the University of Edinburgh in 1923, he filled resident house appointments at Edinburgh Royal Infirmary, St. Luke's Hospital, Bradford, and at Grassington Sanatorium, Yorkshire, until, in 1926, he entered into partnership with Dr. Arthur Lucas and began work in general practice in Bury. He succeeded his principal on Dr. Lucas's retirement in the following year and soon established a reputation as a sound family doctor. Unfit for active service in the last war, he carried the heavy burden of his own large practice and deputized for several of his absent colleagues, who returned to find that during the whole of the war he had kept the most careful clinical notes on all of their patients. Dr. Young was honorary secretary of the Bury Division of the B.M.A. from 1930 to 1932 and chairman of the Division in 1943–4. He was a member of the local medical committee and of the Bury Infirmary hospital board, and for a year after its inception he was a member of the Bury and Rossendale Hospital Management Committee. He was a keen Rotarian, and had attended the weekly luncheon on the day of his death. His leisure hours were spent in gardening. At the funeral service in Bury parish church, where Dr. Young was a sidesman, a crowded congregation gave evidence of a public mourning the loss of a good doctor, a worthy citizen, and a willing friend, who was always ready to offer a helping hand. Our sympathy is extended to his widow and to his son and daughter.

We record with regret the death on March 7 at Johns Hopkins Hospital, Baltimore, U.S.A., of Dr. LIDA OREM MEREDITH at the age of 57. Dr. Meredith was born at Buckeystown, Dorchester County, Maryland, on January 16, 1895, of old British stock, her ancestors from this country having first settled in Maryland 300 years ago. She grew up in an atmosphere of affection for England and a love and admiration for English literature. She was educated at the High School, Cambridge, and at Western Maryland College. After teaching for some years she achieved her aim and started the study of medicine at the Women's Medical College, Philadelphia, but, influenced by an English lecturer, she decided to come to England to study for a year at the Royal Free Hospital. She stayed four years and qualified M.R.C.S., L.R.C.P. in 1934. On returning home she passed the local examinations with distinction and then settled in practice in her home town of Cambridge, where her chief interest was in surgery and obstetrics.

Dr. Catherine E. Orr-Ewing writes: During the 20 years I knew Dr. Meredith she never had a real holiday, but each year would spend some time at Johns Hopkins keeping her knowledge up to date. During those years she collected first editions, original drawings, and manuscripts, and her collection of children's books was exhibited at the Enoch Pratt Library in Baltimore last year. In 1949 and again in 1951 she was operated upon for cancer. During the last years of her life she received citations for her achievements from Hood and Western Maryland Colleges, and she was recognized as one of Maryland's outstanding women. Dr. Meredith was the only woman to serve on the board appointed to investigate maternal and infant mortality in Maryland, and she was the only woman to practise in Dorchester County. Throughout her career she upheld the highest standards of medical ethics. She will be deeply mourned by her colleagues on the staff of Cambridge Hospital, who acted as pall-bearers at her funeral; by her many patients, especially the poor coloured folk, whom she treated free of charge; and by none more than her British friends, who benefited by her friendship, her generosity, and her love for England and the Royal Free Hospital.

By the sudden death from coronary thrombosis on March 14 of Dr. HENRY CHARLES CECIL REID at the early age of 51, Plymouth has lost a highly esteemed member of the profession. The son of a Presbyterian minister, Dr. Reid graduated M.B., B.Ch. at Queen's University, Belfast, in 1923. Soon afterwards he settled in Plymouth, where he engaged in general practice. He was a member of the local medical committee and the executive council, and for many years had served on the panel committee. At one time he had been a city councillor His outdoor recreation was golf, a game in which his proficiency was much above the average. Of a kind and unselfish disposition, he maintained the high ideals of the good type of family doctor, beloved by his patients and popular with his colleagues. A large and representative attendance at the funeral service in Trinity Presbyterian Church mourned his passing. Our sincere sympathy is extended to his widow and daughter in their bereavement.

We record with regret the death of Dr. P. O. ELLISON on March 19 in the Royal Northern Hospital, London, at the age of 60. Philip Oswald Ellison was born on January 30, 1892, and, after winning the junior entrance scholarship in science in 1909, he entered St. Bartholomew's Hospital to receive his medical training, and qualified M.R.C.S., L.R.C.P. in 1916. In the following year he took the degrees of M.B., B.S. of the University of London. After holding an appointment as house-physician at Bart's he was appointed pathologist to the Ministry of Pensions Hospital at Bath in 1920. He then became pathologist to the Fulham General Hospital and later pathologist to the Royal

Northern Hospital, a position which he held at the time of his death.

Dr. Martin Hynes writes: Dr. Ellison had been in robust health only a week before he died, and his sudden loss is acutely felt by his friends. The pathological laboratory at the Royal Northern Hospital was virtually his independent creation, for he had superintended its erection in 1934 from funds provided by the late Philip Hill, and the nucleus of the technical staff had been trained by him. Ellison was the most genial and kindly of men. His two great interests were his laboratory and his garden, and he was never happier than when talking with his colleagues, whether the topic was medicine or roses. He was a clinical pathologist of the old school, never content with an investigation unless he had himself seen the patient, taken the specimen, and performed every detail of the bench work. He had no liking for the post-war pathology, in which a vastly greater demand for laboratory investigations can be met only by delegating most routine work to technicians, and for the last 18 months he had confined himself to morbid anatomy and histology. In these subjects his technical skill found full scope, and every report was of necessity the personal work of the pathologist himself. Paradoxically, it was Ellison's scrupulous technique and insistence on personal work that barred him from academic distinction. In the days between the wars he often worked until midnight to complete himself the routine work of his laboratory, and the talents of a painstaking research worker were thus wasted in the minutiae of unessential investigations. Yet the depth of his knowledge and judgment were clear to all who talked with him, and in one field were displayed to a wider public in the chapter he contributed to Saner's *The Breast*.

Dr. ERNEST TALBOT, who practised in the Longden Dale district, where Cheshire, Yorkshire, Lancashire, and Derbyshire meet, died on March 20 at the age of 63. He was born at Bolton on November 6, 1888, the son of Mr. Thomas Talbot, and was educated at Bolton Grammar School and at the Victoria University of Manchester, where he graduated M.B., Ch.B. in 1913. In his second year as a medical student he was awarded the Professor Tom Jones anatomy scholarship with two bronze medals. After graduation he held the posts of junior and senior house-surgeon at Manchester Royal Infirmary and resident surgical officer at Ashton-under-Lyne Infirmary. On the outbreak of war in 1914 he volunteered for active service and, as a regimental medical officer, was awarded the Military Cross for bravery and devotion to duty. After the war he entered into partnership with the late Dr. G. J. Awburn, in Mottram, where he remained until his death. His tireless efforts on behalf of patients, whom he always treated as friends, made him a well-loved figure in the district. A very good anaesthetist—he became honorary anaesthetist to the Ashton Infirmary—he had the assurance and skill which made his patients feel that they were in good hands. To the meetings of the Hyde Division of the British Medical Association, of which he was chairman in 1936–7, he brought forthright opinions on local and national problems, views which were always refreshing and constructive in their nature. He was also a contributor to the *Journal*. Outside his professional work Dr. Talbot was keenly interested in amateur theatricals, cricket, the local agricultural show, and the British Legion, in which he had many friends. Soon after the end of the war of 1914–18 Dr. Talbot married Miss Mary Harrison, of Ashton, and she and two sons survive him, together with two of his brothers, Dr. Philip Talbot, of Deganwy, Caernarvonshire, and Dr. Geoffrey Talbot, of Prestwich, Manchester.

J. G. B., to whom we are indebted for the above details, writes: We in the Hyde Division of the B.M.A. will miss Ernest Talbot, as he will be missed in Longden Dale, for his cheerful face and encouraging smile which must have spurred on and helped many people through the battle of life. He died after 30 years of self-sacrificing and kindly service among his friends. I have lost a good friend who graduated with me, who was house-surgeon with me, and who volunteered for service in the war of 1914–18 when I did. On return to civil life we practised medicine within five miles of each other, and his death has severed a friendship of 44 years' standing. His life was one of strenuous service and painful illness gallantly borne. There is no one I would rather meet in the hereafter than Ernest Talbot, of Mottram, my good friend and one of Nature's gentlemen.

The medical profession on the south-east coast of England has lost a unique personality by the untimely death on March 22 of Dr. T. D. OVEREND. Thomas Dallas Overend was born at Edmonton, North London, in 1894, the son of Dr. Walker Overend, and was educated at Dulwich College, obtaining an open science scholarship to Christ Church, Oxford, in 1913. After serving in the first world war as a private in France he completed his medical education at University College Hospital, qualifying M.R.C.S., L.R.C.P. in 1920 and obtaining the D.M.R.E. of the University of Cambridge in 1924. After house appointments at University College Hospital and a clinical assistantship in the electrotherapeutic department at St. Bartholomew's Hospital, Dr. Overend became an assistant to his father, one of the pioneers in radiology, and saw his book, *Radiology of the Chest*, through the press in 1928, two years after the death of the author. He followed his father as radiologist to the Buchanan Hospital, St. Leonard's-on-Sea, and was appointed to the similar post at Bexhill Hospital when that institution was opened in 1933. During the last war he was radiologist in the Emergency Medical Service and worked day and night, often assisting at surgical emergencies after having taken the radiographs. When the National Health Service was established Overend was appointed one of the two consultant radiologists to the district, and gave all his time and energy to the work. During the course of his career he published papers on his specialty in this and other journals. For a number of years he was honorary treasurer of the East Sussex Medico-Chirurgical Society, and from 1939 to 1945 he was chairman of the Hastings Division of the British Medical Association. He was a prominent Freemason, and had been Worshipful Master of the St. Leonard's lodge. As a member of the Territorial Army he was for a number of years attached to the Royal Sussex Regiment (Cinque Ports). Overend was a real scholar, and among his many mental endowments was his genuine love of the classics. Although his bodily movements were deliberate and slow, his mind worked like quicksilver. He will be sadly missed, but the memory of his humour, wit, and wisdom will be an abiding joy. He leaves a widow, to whom we extend our deep sympathy.—D. L.

Dr. LEONARD LESLIE, who died on April 7 at the age of 66, was born on January 18, 1886, and was educated at the University of Edinburgh, where he graduated M.B., Ch.B. in 1909, proceeding M.D. two years later. After holding resident posts at the Hospital for Sick Children and at the Royal Infirmary in Edinburgh he settled in practice in Streatley, Berkshire, where he remained until his death, except when he was on service in the R.A.M.C. in France, Salonika, and Palestine in the war of 1914–18, in which he was mentioned in dispatches. Dr. Leslie was at one time president of the Reading Pathological Society and a member of the Berkshire local medical committee and executive council. From 1932 to 1934 he was chairman of the Reading Division of the British Medical Association and was president of the Berks, Bucks, and Oxford Branch in 1934–5. He was medical officer to the Nautical College and St. Andrew's School, Pangbourne, and to Cranford House School, Moulsford.

We are indebted to Sir Robert Hutchison for the following appreciation: Leonard Leslie was an outstanding example of the best type of country practitioner. To sound professional knowledge and a wide experience he added shrewd common sense which made him a most capable family

doctor. Thanks to his wide humanity, moreover, he was always as much interested in the patient (and his relatives) as in the complaint, and where he could not bring healing he never failed to bring comfort and support; while if the disease proved incurable he had the art to smooth the downward path. Being a born doctor, he thoroughly enjoyed his work and never spared himself in it. No summons was ever "mocked by chill delay," and he went his wide rounds every day of the week. During the last war he was, like so many, much overworked, and latterly the only break he allowed himself in the year was a few weeks' fishing and golfing holiday in his native Scotland; it is probable indeed that long-continued overstrain contributed to the final breakdown of an originally strong constitution. The whole of Leslie's professional life was spent in Streatley and its neighbourhood, and during forty-one years of practice there he had become the guide, counsellor, and father confessor of all sorts and conditions of men. I have often heard him say that the first essential in a good doctor was kindness, and this he gave to all his patients in full measure. He was always so cheerful and so bounding in energy and heartiness that his rather unexpected death came with the shock of a personal bereavement to the many who had come to regard him both as a tried friend and as a present help in all times of trouble. All his patients will grieve for him, but special sympathy is due to his daughter and, most of all, to his wife, who through all the difficulties of a doctor's household took such devoted care of him.

Medical Notes in Parliament

NATIONAL HEALTH SERVICE BILL

Amendments Proposed in Committee

On April 3 the Money Resolution authorizing payments under the Bill was reported to the House of Commons.

Mr. ANEURIN BEVAN asked whether a regional hospital board would be entitled to use receipts from charges made for abdominal belts and things of that kind to be set off against the rest of its expenditure.

Mr. H. F. C. CROOKSHANK said that cash recovered through the appliances account would in fact be paid into the Exchequer and would not be set off. How it might be returned and redistributed was another problem. After further debate the Resolution was agreed to.

The House, in Committee, then began discussion of the Bill itself. On Clause 1 (Charges for Certain Drugs, Medicines, and Appliances) Mr. H. MARQUAND moved an amendment that the regulations imposing charges for medicine should lapse before April 1, 1954. This might help to remove the feeling that the Government intended to deal a body blow at the National Health Service.

Dr. H. M. KING said the practical difficulties of administering the Bill would be great. Therefore the Labour Party sought to limit the operation of the Bill for two years. He asked whether the Government believed in a free medical service in principle but not in time of economic crisis.

Mr. CROOKSHANK said that the power to vary the charges or end them by Order in Council was included in Clause 3 (1) of the Bill, as it was in the 1949 Act.

The amendment was rejected by 276 to 263.

Should Hospital Out-patients Pay?

Dr. EDITH SUMMERSKILL moved an amendment designed to exempt out-patients at hospitals from the charge which it was proposed to make on drugs, medicines, or appliances. She said the position of the out-patient was entirely different from that of the ordinary patient. Nobody could charge the out-patient at a hospital with abusing the service: he was there because his doctor had sent him, and he was usually a poor person.

Mr. J. E. POWELL said there was a close connexion between the few in the general practitioners' surgery and the queue in the out-patient department at the hospital. The Select Committee on Estimates had reported last year that the increase in the services rendered to out-patients was partly due to general practitioners sending to hospital patients whom formerly they would have treated in their own surgeries. If the Government attempted to relieve the pressure on the general practitioner without taking corresponding measures in out-patient departments they would only make bad worse in those departments.

Dr. B. STROSS said it was estimated that the total sum which could be attained by the proposals in the clause was about £500,000. Prescriptions for some drugs were very expensive. The cost of prescriptions for "aureomycin" and cortisone might go up to £10 or £15. Towards the cost of such a prescription the patient would presumably pay 1s. For prescriptions which were much cheaper the cost was only a percentage of 1s. A prescription for 12 tablets of phenobarbitone would cost about ½d. He asked if the patient would have to pay 1s. for this.

Miss PATRICIA HORNSBY-SMITH said Mr. Crookshank had already explained that if the cost was less than a shilling the patient would pay less, provided he bought the medicine direct from the chemist and not through the N.H.S.

Miss Hornsby-Smith said the bulk of the prescription charge which it was proposed to levy was covered by legislation passed by the late Government, under which the saving was estimated to be about £12m.

Dr. A. D. D. BROUGHTON said he had supported the proposal in the Bill of 1949 to make a charge of 1s. for each prescription after he had confirmed by conversation with chemists and doctors that there was abuse on the part of some patients, and after he had learned that some doctors were over-generous in issuing prescriptions. The Labour Government, however, had had the courage to say that it found the 1949 Act would not work. The amendment was rejected by 281 to 269.

Charges for Appliances

Consideration of the Bill was resumed in Committee on April 8.

Mr. H. MARQUAND moved to exempt appliances from the charge. He said that with the experts of the Ministry of Pensions, who for 30 years had been responsible for supplying appliances to war pensioners, in charge of the supply of appliances for the Health Services he believed it was not possible for any abuse to creep in. The House was asked to take the risks of people wearing heavy, awkward, and insanitary appliances for the sake of saving £250,000.

Mr. H. F. C. CROOKSHANK said he had pointed out that the Government had no intention of dealing with artificial legs and arms. It was surgical boots and their repair, surgical abdominal supports, elastic hosiery, and wigs which came into the Bill. Only in the case of surgical abdominal supports had he referred to abuse—attempts by patients to get, in effect, ordinary corsets.

Mr. EDWARD EVANS asked the Minister if he would exempt artificial eyes. He said the cost of an artificial eye was almost negligible. Between 7,000 and 8,000 were issued each year, and the total cost was about £16,000 per year. He also asked for an assurance to be put in the Bill that no charge would be made for hearing-aids.

Mr. CROOKSHANK said that the administrative cost of collecting a charge on four classes of appliances would be absolutely minute. The hospitals had said so. Who in the hospitals should do the work was still being discussed.

The amendment was rejected by 291 to 273.

Mr. W. GRIFFITHS said it delighted Mr. Crookshank to see £40m. awarded to general practitioners, yet he found it ethically correct to charge poor people in the way envisaged in this miserable Bill. Mr. IAIN MACLEOD said he was delighted that at long last justice had been done by Mr. Justice Danckwerts to the most important people in the Health Service. Miss JENNIE LEE said she had been bitterly ashamed when her own party was responsible for charging for teeth and spectacles.

Mr. CROOKSHANK said the Government thought it was better not to have exceptions to the clause but to rely on the regulatory power which was given by the Bill. The regulations would afterwards have to come before Parliament.

No Charge to Children

Mr. F. MESSER moved to insert a provision that no charge should exceed one-quarter of its cost to the Minister or the sum of £1, whichever might be the less. He said that a child who was growing up needed different sizes of calliper splints, surgical boots, or spinal jackets as time went on. It seemed to him to be immoral to save money at the expense of those least able to afford it. He pointed out that in the old days voluntary hospitals were unable to be extravagant because they could spend only as much as they collected, and in municipal hospitals the ratepayer had the last word. Those two checks imposed a responsibility in expenditure which did not exist at present. Those who ran the hospitals now did not have complete control of expenditure. If the country had a higher standard of general practitioner it might need fewer hospital beds. There was a wide field for economy in the Health Service.

Dr. B. STROSS, supporting the amendment, said there was a movement away from self-medication which explained part of the increased drug bill.

Miss P. HORNSBY-SMITH said Mr. Messer had wandered wide of the amendment. Mr. Crookshank had no intention of making a charge for spinal jackets and calliper splints. The Bill provided that no charge should be made for appliances for children under 16 or for those attending full-time at school beyond that age.

Mrs. E. M. BRADDOCK asked how a person in receipt of National Assistance was to intimate to chemists, or the doctor who gave a prescription, that he was in receipt of National Assistance.

Miss HORNSBY-SMITH said that anyone could ask for a receipt and would get the shilling back when they presented it at the Post Office with their book showing they were entitled to supplementary pensions. The amendment was rejected.

Full Charges for Foreigners?

Miss IRENE WARD moved to provide that charges for appliances supplied to foreigners should in no case be less than their full cost.

Mr. CROOKSHANK said the amendment would exclude Commonwealth visitors or Irish people, who got the benefits of all other arrangements in this country. It would also exclude foreigners permanently in this country who, although contributors to the Health Service, had not taken out papers of citizenship. He doubted if there was any greater amount of abuse in this matter by foreign nationals. Owing to the abolition of the identity card he could see no easy way of securing firm proof of nationality. Miss Ward's amendment was rejected.

Dispensing Doctors not Tax Collectors

On April 9 Dr. B. STROSS moved that no medical practitioner should be required to make or recover any charge. He quoted from the leading article in the *British Medical Journal* of February 9 saying that the method proposed to collect this money would turn dispensing doctors into tax collectors. The Medical Practitioners' Union also criticized the proposal. Chemists and pharmacists also strongly felt that they should not be dragged in as agents for the collection of money in this way, and Parliament should respect their wishes in this matter.

Dr. A. D. D. BROUGHTON seconded the amendment.

Mr. A. BLENKINSOP said it was a matter of real consequence whether a busy pharmacist should be required to calculate the extra cost of a prescription which was being made up. This applied also to pharmacists making up prescriptions in hospitals or out-patient clinics.

Miss P. HORNSBY-SMITH said arrangements were being worked out with the rural doctors, and she hoped they would be satisfactory for both sides. She did not propose to argue controversial points while these negotiations were progressing smoothly. The amendment was rejected. The Bill was further considered in committee on April 10, and final discussion deferred till after the Easter recess.

Pensions Increase

Mr. OSBERT PEAKE, Minister of National Insurance, on April 8 made a statement on increased benefits and pensions in Great Britain. He said that following discussions with industry the Government had decided to introduce at the earliest possible moment a Bill containing proposals on the lines indicated by the Chancellor of the Exchequer in his Budget statement. These proposals were: (1) an increase in the rate of family allowances from 5s. to 8s. a week; (2) an increase in National Insurance benefits, including unemployment, sickness and widows' benefits and retirement pension, from the present figures of 26s. single and 42s. married to 32s. 6d. single and 54s. married. These higher rates would also be made available to existing pensioners in Great Britain whether they reached pension age before or after October 1, 1951; (3) an increase in the basic rate of industrial injuries benefit from 45s. to 55s.

These proposals would for the first full year cost for family allowances which come out of the Exchequer about £37m. and for National Insurance and Industrial Injuries benefits which come out of the Insurance Funds about £60m. and £3m. respectively. Mr. Peake hoped to bring the new rates of retirement pension into operation at the end of September, family allowances by the beginning of September, and other improvements such as those for sickness and unemployment towards the end of July. The new rates of contribution would become payable in October.

On April 9 Mr. D. HEATHCOAT-AMORY recalled that Mr. Butler had announced in his Budget speech an increase from 45s. to 55s. a week (officers £26 a year) on the standard basic rate of disability pension for 100% disablement, with proportionate increases for lower assessments. This improvement would take effect from the first pay-day in May and would apply to about 695,000 pensioners.

With effect from the first pay-day in May the standard rate of 35s. payable to a widow over 40, or receiving an allowance for a child, or incapable of self-support, would be increased to 42s. The amount of the increase for comparable widows of officers will be £18 a year. The new rates benefited about 150,000 widows of both world wars. Both disablement and widows' pensions were being revised. It had been decided to increase from £52 10s. to £57 a year the allowance towards maintenance and running expenses paid to those severely disabled war pensioners supplied with motor-cars by the Ministry.

Hospital Admission for the Senile

A Bill to permit in Scotland the reception and maintenance in mental hospitals and similar institutions of senile persons without certification of insanity or lunacy was introduced by Mrs. JEAN MANN on April 8 and was read a first time.

Teething Powders

On April 10 Mr. J. B. HYND asked the Minister of Health whether he would make inquiries into the effects on children's health of the widespread use of teething powders containing mercury and give publicity to the result of his inquiries.

Miss P. HORNSBY-SMITH replied. She said inquiries were in progress at various children's hospitals. Although indiscriminate use of teething powders was clearly undesirable, there was not yet definite evidence to justify general publicity.

The Doctor's Income

Replying on April 9 to Dr. S. HASTINGS, Mr. H. F. C. CROOKSHANK stated that the average number of principals providing medical services under Part IV of the National Health Service Act in the year ending March 31, 1951, was

17,717. These were not paid salaries, but their total remuneration for such services, including the value of the Exchequer superannuation contributions, was £43,506,262. This represented an average of £2,456 per doctor, out of which he had to meet his professional expenses.

Average Capitation Fee.—In the year ending March 31, 1951, the average payment, based on an annual capitation fee of 18s., was just under 16s. 5d.

Universities and Colleges

ROYAL COLLEGE OF SURGEONS OF ENGLAND

At a meeting of the Council of the College held on April 3, with Sir Cecil Wakeley, President, in the chair, it was announced that the College had been adjudged by the House of Lords to be a charity, in a case arising out of the will of the late Lady E. G. Bland-Sutton. A bequest to the College from Mrs. Eliza Handcock, of Bournemouth, was reported to the Council.

Mr. G. T. W. Cashell, F.R,C.S.Ed., was elected to the Fellowship of the College *ad eundem*. The following were elected Fellows of the College without examination as being medical practioners of at least 20 years' standing: Mr. E. H. Shaw, Mr. S. A. Henry, Mr. V. B. Green-Armytage, Sir William Kelsey Fry, Mr. A. J. Boase, Professor J. Kirk.

The Jacksonian Prize for 1951 was awarded to Mr. Rodney Smith (St. George's) and a certificate of honourable mention was awarded to Mr. Oliver Jelly (Manchester). The Council selected "Pathology and Surgery of Peripheral Vascular Occlusion" as the subject for the Jacksonian Prize for 1953.

The John Hunter Medal and Triennial Prize were awarded to Dr. Cuthbert E. Dukes for his outstanding contributions to pathology in general, with special reference to his work on cancer.

A Leverhulme Research Scholarship was awarded to Mr. J. N. Ward-McQuaid, and Mr. D. I. Williams's Leverhulme Research Scholarship was renewed for a further year.

The Begley Prize for 1952 was awarded to Miss J. R. C. Jones (Charing Cross Hospital).

Diplomas in Tropical Medicine and Hygiene, in Ophthalmology, in Physical Medicine, and in Child Health were granted, jointly with the Royal College of Physicians of London, to the following successful candidates:

DIPLOMA IN TROPICAL MEDICINE AND HYGIENE.—M. A. Baddoo, K. L. Batten, R. A. Benninger, B. Bevan, C. Bianchini, Elizabeth R. Bridgman, P. A. Cooper, R. E. Davenport, T. Derola, E. M. Ensor, J. G. Grounds, N. R. Gupta, C. R. Jones, V. N. Kapur, S. A. Karimjee, K. B. Kenyon, P. K. K. Knudsen, A. H. Laxton, G. S. Mahapatra, M. G. Mandavia, D. Metselaar, D. O'Keeffe, J. G. Paranjpe, R. F. Payne, M. A. A. Razek, H. A. Reid, L. R. Roberts, Kathleen C. Rogers, J. Schneider, F. D. Schofield, B. M. A. Shafik, P. A. Shave, S. Skulthai, C. Sudhipongse, W. R. G. Thomas, W. R. W. West-Watson.

DIPLOMA IN OPHTHALMOLOGY.—J. D. Brosnan, P. A. Clarke, R. R. Collmann, Teresa Coyle, Gwenllian Edwards, W. S. Foulds, P. Griffiths, J. W. Hornbrook, E. G. Hurd-Wood, A. S. Jones, S. B. Kapur, J. K. McCall, B. M. McOwan, R. J. Patel, Rhona A. Reid, C. W. Thornhill, Dorothy F. Usher, M. P. van Huyssteen, C. H. Walsh.

DIPLOMA IN PHYSICAL MEDICINE.—D. C. Arnott, L. B. Blomfield, J. Fulton.

DIPLOMA IN CHILD HEALTH.—Anne M. Allen, J. D. Allen, Marion M. Ashforth, Honor E. Bambridge, Alice Benjamin, D. U. Bloor, D. S. N. Brierley, J. G. S. Buchanan, G. J. Budow, June D. Cain, W. H. Cary, P. Catzel, Rachel Chacko, Jean E. H. Charlton, D. N. Chatterji, P. R. Clay, Nancy Cole, S. V. Cullen, Lorna C. Davies, Sheila F. Dawson, D. J. Dobson, S. E. Ellison, R. J. Fassina, Mary E. G. Feetham, B. M. Fehler, A. Freedman, S. Freier, L. Friedlander, N. A. W. Gibson, N. Goldblatt, Irene Harrison, M. M. Hassan, J. P. de V. Hendrickse, Susan E. Herdman, Catherine M. Hoyle, T. T. S. Ingram, Brenda James, E. H. Judge, S. M. Kaplan, Irene E. Kenmuir, Margaret M. Kerr, D. K. Kouyoumdjian, Janet M. Lamont, S. G. Loh, G. M. Lurie, Isabel M. McCullough, Bridget M. V. McGettigan, Mary B. B. McGregor, Kathleen G. McKee, Elisabeth Monkhouse, N. M. Newman, G. A. Perling, H. T. Phillips, Dorothy E. M. Pierce, Jill Poole, Megan C. Pratt, D. H. H. Pullon, H. G. Rischbieth, Margaret Rogers, N. R. Rowell, Olive Sharpe, Freda Sheinbaum, N. Sher, Joan Slack, A. L. Speirs, F. A. Springall, H. Stein, Janet M. Stokes, Hilda J. Tanner, J. B. Taylor, R. MacN. Thomson, Sheila M. Tyrrell, S. Vakil, H. K. Virik, J. R. H. Watson, J. N. Wattie, Hebe F. Welbourn, R. H. R. White, Constance M. Wilkinson, Olive C. Wilks, Mary E. S. Wylie, V. C. G. Yzelman.

The following hospitals were recognized under paragraph 23 of the F.R.C.S. regulations: Bulawayo Government Hospital, two senior house-surgeons. Salisbury General Hospital, Southern Rhodesia, two senior house-surgeons. Heatherwood Orthopaedic Hospital, Ascot, two orthopaedic registrars, for six months. Westwood Hospital, Beverley, Yorkshire, house-surgeon and orthopaedic house-surgeon, both for six months. Gulson Hospital, Coventry, resident surgical registrar, resident surgical officer, both for six months. East Riding General Hospital, Driffield, house-surgeon for six months (till March 31, 1954). West Middlesex Hospital, Isleworth, four house-surgeons in general surgery, for six months; three surgical registrars, for one year; house-surgeon (orthopaedic), for six months (decennial revision). Kettering and District General Hospital, house-surgeon and casualty house-surgeon, both for six months. Leicester Royal Infirmary, registrar, ear, nose, and throat department (under paragraph 23c of the regulations). Macclesfield Hospital, surgical registrar, senior house officer, both for six months. Neath General Hospital, resident surgical officer, for one year; two house-surgeons, for six months. Newcastle-upon-Tyne General Hospital, two surgical house officers (general surgery), for one year; two house-surgeons (general surgery), for six months. Staffordshire General Infirmary, Stafford, resident surgical officer and house-surgeon, both for six months. Swansea General Hospital, resident surgical officer, for one year; two registrars, both for one year; three house-surgeons in general surgery, for six months (decennial revision).

Vital Statistics

Smallpox in Lancashire

Four cases of variola minor were notified in the week ending April 12—Rochdale 1, Littleborough 2, and Wardle 1. The diagnosis of the Wardle case is not certain. No more cases have been reported from Aldershot. The total of cases to April 12 is 136.

Week Ending April 5

The notifications of infectious diseases in England and Wales during the week included: scarlet fever 1,361, whooping-cough 3,004, diphtheria 22, measles 6,836, acute pneumonia 711, acute poliomyelitis 19, dysentery 548, paratyphoid fever 7, typhoid fever 1.

Quarterly Return for Scotland

The birth rate, 16.1 per 1,000, during the fourth quarter of 1951 was the lowest rate since 1940. The infant mortality was 36 per 1,000 registered live births; it was 6 below the rate for the corresponding quarter of 1950 and 13 below the average of the five preceding fourth quarters. The general death rate was 11.5 per 1,000; this was 1.6 below the rate for the last December quarter and 0.9 below the five-years average. Deaths attributed to the principal infectious diseases numbered 45, and of these 22 were due to influenza, 11 to whooping-cough, and 7 to cerebrospinal fever.

A large fall was recorded in the death rate from tuberculosis. The death rate from all forms of tuberculosis was 37 per 100,000, and that from respiratory was 33. The former rate was 14 and the latter 13 below the rate for the corresponding quarter of 1950, and they were respectively 32 and 28 below the five-years average.

The preliminary report for the whole year shows that the birth rate in 1951 was 17.7 per 1,000 of the population; this rate was 1.9 below the average of the five preceding years and the lowest rate since the war, being the same as the average for 1935–9. Infant mortality was 37 per 1,000 live births—this rate was 2 below that for 1950 and was the lowest infant mortality ever recorded in Scotland. The general death rate was 12.9 per 1,000 of the population, and it was 0.5 above the rate for 1950 and the average of the five preceding years. Deaths from epidemic diseases

numbered 1,132 compared with 605 in the preceding year, the increase being due mainly to influenza, which accounted for 950 deaths against 386 in 1950. Other deaths in this classification included 98 from whooping-cough (compared with 61 in 1950), 44 from cerebrospinal fever, and 24 from acute poliomyelitis. Five deaths were attributed to diphtheria, 2 more than in 1950. Only 1 death was recorded from scarlet fever, the smallest number ever registered in Scotland. The death rate from all forms of tuberculosis was 43 per 100,000, and that from respiratory tuberculosis was 37; these rates were 28 and 23 below the average of the five preceding years.

Infectious Diseases

Only small variations occurred in the returns of infectious diseases in England and Wales during the week ending March 29. The largest were increases in the number of notifications of measles by 68 and dysentery by 76, and a decrease of 83 for scarlet fever.—

The fall in the incidence of scarlet fever was mainly in the south-eastern counties; elsewhere in the country the trend was almost unchanged. The largest variations in the local trends of measles were decreases in Yorkshire East Riding 170 and Cheshire 142, and an increase in Lancashire 103. The returns of whooping-cough showed the usual fluctuations of this disease. The largest was a decrease of 48 in the notifications of Lancashire. The notifications of diphtheria were 4 fewer than in the preceding week. Five further cases of diphtheria were notified from the outbreak in Lancashire, Darwen M.B.

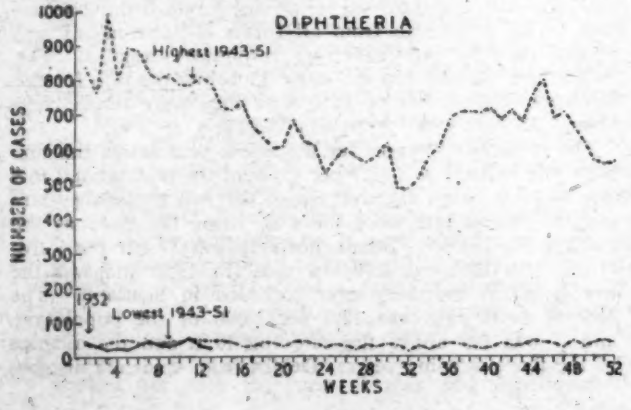
The number of notifications of paratyphoid fever was 6 more than in the preceding week. The largest outbreak during the week involved 5 persons in Bristol C.B.

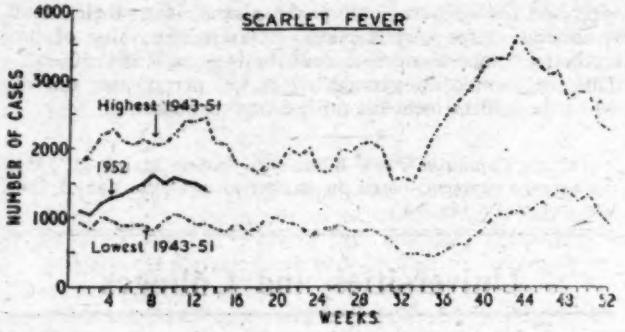
The notifications of acute poliomyelitis were 2 fewer for paralytic cases and 6 fewer for non-paralytic cases than in the preceding week; the notifications were the lowest recorded in any week for almost three years. The counties with multiple notifications during the week were Kent 3, Bucks, Aylesbury R.D. 2, Yorkshire West Riding 2.

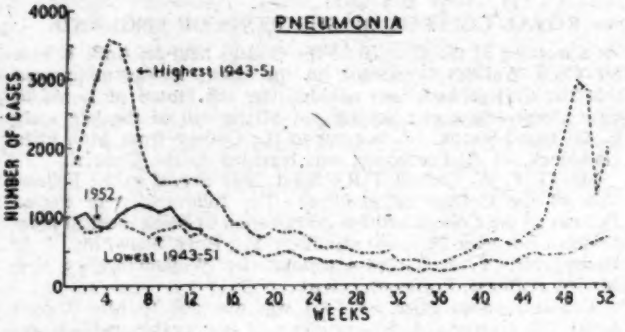
The chief features of the returns of dysentery were rises in Lancashire 33 and London 21. The largest returns during the week were Lancashire 150 (Oldham C.B. 62, Farnworth M.B. 16, Chadderton U.D. 13), Middlesex 90 (Enfield U.D. 39, Edmonton M.B. 20, Ealing M.B. 12), London 70 (Finsbury 10, Hackney 10), Norfolk 40 (Norwich C.B. 30, Depwade R.D. 10), Northumberland 32 (Ashington U.D. 18, Newburn U.D. 11), Berkshire 28 (Maidenhead M.B. 12, Abingdon R.D. 11), Staffordshire 24 (Uttoxeter R.D. 11, Lichfield R.D. 10), Leicestershire 21, and Surrey 20.

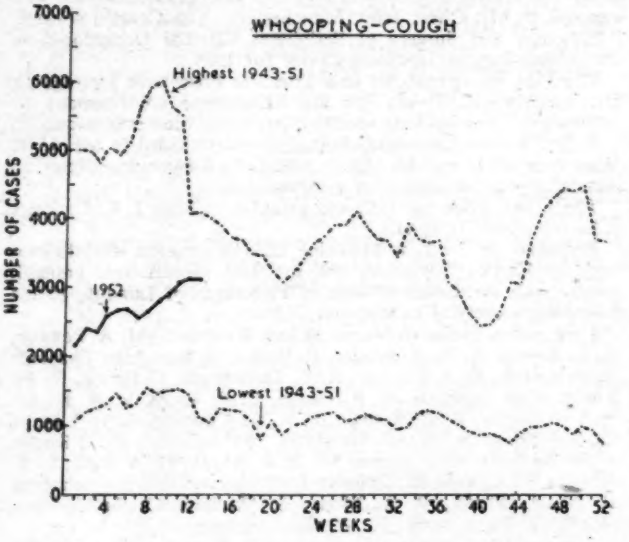
Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported during the nine years 1943–51 are shown thus - - - - - - - -, the figures for 1952 thus ————. Except for the curves showing notifications in 1952, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.









First Quarter of 1952

No exceptional trends occurred in the incidence of infectious diseases in England and Wales during the first quarter of this year. The number of notifications of diphtheria was the lowest ever recorded. The rate of decline of this disease is falling, and apparently the trend will soon flatten out near the base line. The mortality from influenza in the great towns was very low. The number of notifications of dysentery was about half that recorded in the first quarter of last year, but the incidence of this complaint remains at a very high level. A comparison with the notifications of the four preceding years is as follows:

England and Wales	1948	1949	1950	1951	1952
Scarlet fever	23,348	16,087	24,802	12,088	18,013
Whooping-cough	35,034	37,221	23,619	66,865	35,042
Diphtheria	2,466	1,523	955	572	456
Measles	88,489	201,140	54,368	311,709	64,596
Acute pneumonia	10,969	17,147	13,720	26,536	12,960
Meningococcal infection	629	479	536	662	562
Acute poliomyelitis	417	245	512	339	288
Dysentery	2,100	886	3,938	13,995	6,936
Enteric (typhoid and paratyphoid)	103	100	154	149	126
Great towns:* Influenza deaths			1,201	7,899	485

* 160 great towns in 1952, 126 formerly.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **March 29** (No. 13) and corresponding week 1951.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the 160 great towns in England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1952					1951				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	29	5	13	0	3	46	3	16	1	2
Dysentery	592	70	67	1	2	999	147	212	18	
Encephalitis, acute	6	0	0	0		4	0	0	0	
Enteric fever:										
Typhoid	1	0	0	0		7	0	0	0	3
Paratyphoid	12	0	1 (B)	0		21	0	1 (B)	0	
Food-poisoning	65	9		33		88	9		0	
Infective enteritis or diarrhoea under 2 years				7	12				12	15
Measles*	6,953	270	588	317	476	31,268	2360	336	131	104
Meningococcal infection	38	4	32	0	3	58	3	19	2	3
Ophthalmia neonatorum	32	3	16	0		20	0	10	0	
Pneumonia†	801	39	400	8	4	909	48	239	10	4
Poliomyelitis, acute:										
Paralytic	10	1	3	0	3	19	0	2	0	
Non-paralytic	2	0				4	0			
Puerperal fever§	268	45	17	3		62	2	7	2	1
Scarlet fever	1,403	110	176	18	59	918	61	143	24	61
Tuberculosis:										
Respiratory			170	18				171	13	
Non-respiratory			30	1				32	4	
Whooping-cough	3,110	146	262	87	48	4,098	198	557	25	59

DEATHS in Great Towns	1952					1951				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire	Eire
Diphtheria	0	0		0	0	*1*	0	*0*	0	0
Dysentery	1	0		0		-	1		0	
Encephalitis, acute		1			1		0			0
Enteric fever	0	0	0			-				
Infective enteritis or diarrhoea under 2 years	11		0	0	1	*17*		*1*	0	0
Influenza	34	4	16	0	2	*64*	8	*0*	0	3
Measles		0	2	0	1		4	*1*	0	0
Meningococcal infection		2					0	*3*		
Pneumonia	282	25		7	4	*289*	40		11	9
Poliomyelitis, acute	1	1			0	*2*	0			0
Scarlet fever		0		0	0		0	*0*	0	0
Tuberculosis:										
Respiratory	119	21	25	3	9	*152*	31	*35*	7	17
Non-respiratory		1	3	0	1		4	*3*	0	4
Whooping-cough	0	0		0	1	*4*	0	*3*	0	0
Deaths 0–1 year	257	28	33	9	14	*311*	39	*43*	17	24
Deaths (excluding stillbirths)	5,294	756	661	101	183	*5,826*	910	*691*	152	209
LIVE BIRTHS	7,766	1188	863	202	381	*7,696*	1236	*999*	247	476
STILLBIRTHS	206	19	29			*199*	30	*29*		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Medical News

The Listerian Festival.—The Listerian Festival is held every three years on a date as near as possible to April 5 (Lord Lister's birthday). This year the Lister Oration, the tenth, was given on April 4 at the Royal College of Surgeons by Sir James Learmonth, who spoke on a theme which he entitled, "After 56 Years." Later in the same day the Listerian Festival Dinner was held at the College, where the guests were received by the President, Sir Cecil Wakeley. The main toast of the evening, that to the Royal College of Surgeons, was proposed in a brief and witty speech by the Minister of Health, Captain Harry Crookshank, who said that his relationship with the Royal Colleges was a most happy one. He referred, as did Sir Cecil Wakeley when responding to the toast, to the previous day's ruling in the House of Lords that the College was a charity. Sir Cecil described this judgment as "a welcome recognition of our status as a scientific and educational body and a very present help in our perpetual troubles with the Chief Inspector of Taxes." After speaking of the affairs of the College in 1880, the year Lister became a member of its council, Sir Cecil reported on the rebuilding of the College which is now in progress, and said that it would be reasonable to hope that the Great Hall of the new building would be ready for the next Listerian Festival in 1955. Proposing the health of the guests, Mr. Philip Mitchiner singled out for special mention two past presidents, Sir Hugh Lett and Lord Webb-Johnson, who had in the past done noteworthy work on the College's behalf, and two direct descendants of Lord Lister, "who carry on in the medical profession the tenets which Lister taught us to obey and respect." Lord Simonds, the Lord Chancellor, and Dr. A. L. Geyer, the High Commissioner for South Africa, spoke in reply. The toast to the Lister Orator was proposed by Sir James Paterson Ross, who described the Oration as a substantial, elegant, and enduring contribution to the treasure of oratory of which the College was so proud. Sir James Learmonth made a brief reply.

Dangerous Drugs on Television.—An hour's programme from Alexandra Palace on Wednesday, April 9, showed dramatically how drug addicts are sometimes caught and cured. A girl is brought into hospital after a road accident with a broken ankle but with no sense of pain and with many needle scars on her arm. She is suspected to be an addict, and when morphine is withheld she becomes very distressed, breaks down, and agrees to be treated. The scene then shifts to the search for her supplier, through the help of the Home Office Drugs Branch. This is the first time the subject, which is of growing social importance, has been treated on B.B.C. television. It was extremely well done, and all the details of medical work were so convincing that it was impossible to believe that the scenes were not being relayed from some actual hospital. This verisimilitude doubtless owed much to the fact that the author of the script, Cormac Swan, is a doctor, at present assistant editor of *Family Doctor*.

Gift for Poliomyelitis Research.—The sum of £1,000 has been given to the Institute of Orthopaedics for the support of research in poliomyelitis. The donors, who wish to remain anonymous, lost a young friend some months ago from a rapidly fatal attack of the disease.

West African Medical Journal.—This journal, started in 1927 and suspended in 1938, is now to be published quarterly. The editor is Dr. D. B. Jelliffe. The journal can be ordered through the London office, Effingham House, Arundel Street, W.C.2, and costs one guinea per annum.

Emergency Bed Service: Applications and Admissions.—During the seven days ending April 14 the number of applications made by doctors to the London Emergency Bed Service for admission of patients was 961, of whom 91.90% were admitted.

COMING EVENTS

Annual Convention of Chiropodists.—This year the meeting of the Society is at the Midland Hotel, Manchester, on April 24, 25, 26, and will be opened by Sir John S. B. Stopford. The convention fee is 10s. 6d., but students may obtain free tickets of admission through their medical schools.

Harveian Society of London.—The Buckston Browne–Gray Hill Dinner of the Harveian Society of London will be held at the Royal College of Surgeons of England, Lincoln's Inn Fields, London, W.C.2, on Thursday, May 15, at 7.30 for 8 p.m.

British Association Annual Meeting.—The next annual meeting of the British Association will be held in Belfast from September 3 to 10 under the presidency of Professor A. V. Hill. Copies of the preliminary programme and full details may be obtained from the association, Burlington House, London, W.1.

International History of Medicine Society.—The 13th congress will be held at Nice, Cannes, and Monaco from September 8 to 14. The registration fee will be 5,000 francs (3,000 for members of the society), and full details may be obtained from M. Jean-Paul Faure, 38, Avenue Auber, Nice.

First International Congress of Neuropathology.—This will be held at Rome, September 8–13. The final programme will shortly become available, and those who wish to join the British party to the congress should communicate with Dr. J. G. Greenfield, at the National Hospital, Queen Square, W.C.1, as soon as possible.

Course in Care of Elderly.—The National Old People's Welfare Committee is organizing another course for those who want to become wardens of homes for old people. The course will last four months, starting in October. Applications are invited by the secretary, 26, Bedford Square, W.C.1.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Monday, April 21

●HUNTERIAN SOCIETY.—At Talbot Restaurant, 64, London Wall, E.C., 7 for 7.30 p.m., annual general dinner-meeting; *"Hunteriana—Part II,"* by Mr. C. Robert Rudolf.

ROYAL EYE HOSPITAL, St. George's Circus, Southwark, London, S.E.—5 p.m., *"Science and Art of Refraction: Introductory,"* by Dr. T. H. Whittington.

Tuesday, April 22

EDINBURGH UNIVERSITY: FACULTY OF MEDICINE.—At Anatomy Lecture Theatre, University New Buildings, Teviot Place, 5 p.m., *"Plastic Changes in the Reflex Responses of the Mammalian Spinal Cord,"* Macarthur Postgraduate Lecture by Professor J. C. Eccles, D.Phil., F.R.S. (Otago).

ROYAL EYE HOSPITAL, St. George's Circus, Southwark, London, S.E.—5 p.m., *"Genetics in Ophthalmology,"* by Professor A. Sorsby.

Wednesday, April 23

FARNBOROUGH HOSPITAL, Kent.—5.30 p.m., clinical meeting. *"Carcinoma of the Lung,"* by Mr. T. Holmes Sellors.

OXFORD UNIVERSITY.—At Radcliffe Infirmary, 5 p.m., *"The Clinical Approach to the Problem of Malignant Cervical Glands,"* Litchfield Lecture by Mr. W. R. Douglas.

ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fields, London, W.C.—5 p.m., *"Tuberculosis of the Urinary Tract,"* Urology Lecture by Mr. Hugh Donovan.

ROYAL EYE HOSPITAL, St. George's Circus, Southwark, London, S.E.—5.30 p.m., *"Ophthalmic Injuries,"* by Mr. L. H. Savin.

ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE, 28, Portland Place, London, W.—3.30 p.m., *"The Avoidance of Injury to Children at Play"* (Illustrated), by Dr. Mary D. Sheridan.

ROYAL MICROSCOPICAL SOCIETY, Tavistock House South, Tavistock Square, London, W.C.—5.30 p.m., *"The Flying Spot Microscope,"* by Mr. F. Roberts, M.Sc.

Thursday, April 24

ALFRED ADLER MEDICAL SOCIETY.—At 11, Chandos Street, London, W., 8 p.m., symposium: *"Essentials of Individual Psychology"*; speakers, Professor R. Dreikurs (recorded in Chicago), Dr. N. R. Beattie, and Dr. J. Bierer. A discussion will follow.

LONDON COUNTY MEDICAL SOCIETY.—At St. James' Hospital, Ouseley Road, Balham, S.W., 3 p.m., clinical meeting.

MANCHESTER MEDICAL SOCIETY: SECTION OF ANAESTHETICS.—At Staff House, Manchester University, 8.15 p.m., *"Anaesthesia in Cardiac Surgery,"* by Dr. E. S. N. Fenton; *"The Description of a Simply Constructed Mechanical Respirator (Spiro-Pulsator),"* by Dr. J. R. Esplen.

PHYSICAL SOCIETY: LOW TEMPERATURE GROUP.—At Science Museum, South Kensington, London, S.W., 5.30 p.m., *"Effect of Low Temperatures on Biological Systems,"* by Dr. J. C. Fidler.

RENAL ASSOCIATION.—At Ciba Foundation, 41, Portland Place, London, W., 4.30 p.m., *"The Nature of the Disintegration of Homo-transplanted Kidneys in Dogs,"* by Dr. W. J. Dempster; *"Auto-regulation of the Renal Circulation,"* by Drs. H. E. de Wardener and B. E. Miles.

ROYAL ARMY MEDICAL COLLEGE.—At Lecture Theatre, John Islip Street, London, S.W., 5 p.m., *"Arthroplasty,"* by Mr. St. J. D. Buxton.

ROYAL EYE HOSPITAL, St. George's Circus, Southwark, London, S.E.—5.30 p.m., *"Post-operative Complications and their Management,"* by Miss J. M. Dollar.

ST. ANDREWS UNIVERSITY.—At Materia Medica Department, Medical School, Small's Wynd, Dundee, 5 p.m., *"Plastic Changes in the Reflex Responses of the Spinal Cord,"* by Professor J. C. Eccles, D.Phil., F.R.S. (Otago).

ST. GEORGE'S HOSPITAL MEDICAL SCHOOL, Hyde Park Corner, London, S.W.—5 p.m., lecture-demonstration in psychiatry by Dr. D. Curran.

ST. JOHN'S HOSPITAL DERMATOLOGICAL SOCIETY, Lisle Street, Leicester Square, London, W.C.—4.15 p.m., demonstration and discussion of clinical cases.

WEST END HOSPITAL FOR NERVOUS DISEASES.—At 48, Cosway Street, Marylebone Road, London, N.W., 5.30 p.m., *"Physical Methods of Treatment.—I"* (Demonstration), by Dr. E. H. Larkin.

WESTMINSTER MEDICAL SCHOOL, Meyerstein Lecture Theatre, Horseferry Road, London, S.W.—5.30 p.m., clinico-pathological demonstration. Discussion: *"Electrolyte Therapy in Surgery"*; speakers will include Professor N. F. Maclagan, Dr. R. D. Tonkin, Mr. A. G. Jessiman, and Dr. C. F. Scurr.

Friday, April 25

INSTITUTE OF LARYNGOLOGY AND OTOLOGY, 330, Gray's Inn Road, London, W.C.—4.30 p.m., general practitioners' meeting. *"Deafness and Hearing-aids,"* by Mr. F. W. Watkyn-Thomas.

MEDICAL SOCIETY FOR THE STUDY OF VENEREAL DISEASES, 11, Chandos Street, London, W.—7.30 p.m., general meeting. Presidential address: *"My Recent Experiences and Problems."* A discussion will follow.

●SOCIETY OF CHEMICAL INDUSTRY: FOOD GROUP.—At Winter Gardens, Margate, 9.30 a.m., joint meeting with Royal Sanitary Institute. *"Bacteriological Standards for Perishable Foods,"* address by Professor H. D. Kay; papers by Mr. W. Price-Davies, B.Sc., A.R.I.C., Mr. C. L. Heller, Ph.C., Mr. A. Rowlands, B.Sc., and M. Ingram, M.A., Ph.D., and J. Brooks, B.Sc., Ph.D. A discussion will follow.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Halpern.—On March 14, 1952, at Chase Farm Hospital, Enfield, Middlesex, to Ruby May (formerly Francis), wife of Dr. M. Halpern, a son—Mark Francis.

DEATHS

Acton.—On April 3, 1952, Thomas Acton, M.R.C.S., L.R.C.P., of 69, Nutfield Road, Thornton Heath, Surrey, formerly of Abbots Bromley, Staffs.

Callender.—On April 3, 1952, at Tentercroft, Cuckfield, Sussex, Eustace Maude Callender, C.B.E., M.D., aged 87.

Fleming.—On April 3, 1952, at his home, 65, Warren Drive, Surbiton, Surrey, Robert Hood Fleming, M.B., F.R.C.S., aged 62.

Mills.—On April 6, 1952, at 35, Surrey Street, Norwich, Robert James Mills, M.B., C.M., aged 96.

Pentony.—On April 4, 1952, at 26, Park Road, Middlesbrough, John Joseph Kevin Pentony, M.B., Ch.B.

Reid.—On April 8, 1952, in hospital, Harriet Rowland Louise Reid, M.B., Ch.B., late of Ashley Lane, Moston, Manchester.

Ronaldson.—On April 5, 1952, at St. Andrew's Hospital, Northampton, James Bruce Ronaldson, O.B.E., V.R.D., M.D., of Innisfree, Little Chalfont, Bucks, aged 66.

Rosenberg.—On April 5, 1952, Hans Willy Rosenberg, M.D., of 108, Greencroft Gardens, London, N.W.

Smith.—On April 5, 1952, at Marley Cottage, Sidmouth, Devon, Edward Protheroe Smith, M.R.C.S., L.R.C.P., aged 77.

Taylor.—On April 3, 1952, at his home, 177, Victoria Road, Thornton, Blackpool, George Taylor, M.B., Ch.B.

Tirard.—On April 4, 1952, at 85, Sloane Street, London, S.W., Nestor Seppings Tirard, M.B., B.Ch.

Any Questions?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

Tuberculosis and Breast-feeding

Q.—*Should mothers with quiescent tuberculosis of the lungs or elsewhere be allowed to breast-feed their babies? If so, what standards of quiescence would be regarded as satisfactory?*

A.—It is not possible to give an unequivocal answer to this question, as there are so many factors affecting the decision. The basic point is that breast-feeding is a severe additional strain on the mother, and whether or not it should be allowed must depend on: (*a*) the time for which the tuberculosis, of the lungs or elsewhere, has been quiescent; (*b*) the social circumstances, especially the home conditions, the number of other children for which the mother has to be responsible, and the amount of domestic help she is able to obtain.

In general, one would advise against breast-feeding within two years of discharge from a hospital, when a patient has an artificial pneumothorax or a pneumoperitoneum, or within a couple of years of either of these being abandoned, but this is a very rough guide. If it is borne in mind that the main factor is avoidance of additional strain, a decision can probably be arrived at in the individual case.

Post-mortem and Ante-mortem Caesarean Section

Q.—(*a*) *How quickly after death must a caesarean section be performed to save the life of the foetus? What signs of death must be present before the section may be begun? (b) In the case of a certainly dying woman, is it justifiable to carry out the section before death, if both she and her husband agree, in order to give the foetus a better chance of survival?*

A.—(*a*) When death follows a prolonged illness, and takes place slowly, the foetus usually dies before the mother. So the circumstances suitable for post-mortem caesarean section arise but rarely, and then when a comparatively fit woman dies suddenly. Sudden death usually means it is unexpected, so there is no opportunity to seek the permission of the husband or other relative. The woman cannot be said to be dead until both respiration and circulation have ceased, and thereafter the child must be delivered within a few minutes if it is to survive. The quicker the mother's death the longer the interval, but according to published records the outside limit is 20 minutes.

(*b*) Caesarean section carried out to recover a live child from a dying woman has been carried out occasionally since at least 1603, but is generally abhorrent to both medical attendant and relatives. It is a proper procedure according to the Roman Catholic faith, but it is difficult to reconcile with the principles governing medical practice, since the operation must almost always hasten and even precipitate the woman's death. It should never be undertaken without obtaining several medical opinions to the effect that death of the woman is imminent, and without clear evidence that the foetus is alive and in good condition. In the circumstances envisaged the woman herself would be in no state to give her consent to the operation, and it is therefore essential to have the written consent of the next of kin. Moreover, it is not permissible to depart from the basic standards of surgical technique and asepsis, because it is just possible the apparently dying woman may recover: such an occurrence is recorded.

Legal Aspects of Post-mortem Caesarean Section

Q.—*Can a husband legally refuse permission for a post-mortem caesarean section when his wife is about to die but the foetus is viable?*

A.—The question is most complicated, and there appears to be no settled law on the subject. It seems clear that as long as the wife is alive she must decide whether an operation should be performed or not, and, if she should be unable to give consent on account of her condition, then consent would be a matter for her husband. If the husband refused, it is very doubtful indeed whether the surgeon could legitimately perform the operation against the husband's will.

After the death of the woman the circumstances are altered. In England there is no property in a dead body, and I understand that theoretically no action would lie if a caesarean section were performed without the consent of the husband. In Scotland, however, there is some doubt whether there is property in a dead body, and there is an old reported case on a charge of theft of a dead body. The modern view, however, appears to be that a husband or next of kin would more probably be looked upon as merely the lawful custodian of the body.

If the body were in the husband's home I feel that morally the doctor should perform the operation even against the husband's will. If the doctor did so, I doubt very much whether he would be liable in any actionable wrong so far as the husband is concerned. If the doctor did not perform the operation as the result of the husband's refusal to consent and the child died *in utero* I do not think that the husband could be charged with any crime, as, so far as England is concerned, this would probably not be "a wilful act within the meaning of the Infant Life Preservation Act, 1929, Section 1." This statute does not apply to Scotland, but I doubt very much if the Common Law in Scotland would embrace a negative act of mere refusal which prevented the possible birth of a live child. If the mother died in hospital, however, I feel that the hospital authorities might perform the operation, assuming consent without waiting for an opportunity to consult the husband, and I cannot see that he would have any recourse in law against those concerned.

High Urinary Ketosteroids

Q.—*What is the significance of a high ketosteroid level in the urine? I have a female patient of 23 who has suffered from hirsutism since puberty; on four separate occasions her urinary ketosteroids have been between 22 and 37 mg. per 24 hours. What is the likely explanation, and what further investigations, if any, are indicated?*

A.—A high level of neutral 17-ketosteroids in the urine of women is indicative of increased production of androgens by the adrenal cortex. In cortical hyperplasia values up to 50 or 60 mg. per 24 hours may be found, but in cortical carcinoma the excretion may be much higher, values over 1,000 mg. per 24 hours having been recorded. The β fraction, which is precipitable by digitonin and consists mostly of dehydro*iso*androsterone, does not normally exceed 10–15% of the total neutral 17-ketosteroids; in carcinoma of the cortex it makes up a considerably larger proportion of the total.

In the case described, the excretion of 22–37 mg. per 24 hours is certainly suggestive of a mild degree of adrenocortical hyperfunction. Other investigations which may prove useful are estimation of the excretion of glycogenic corticoids (as reducing or formaldehydogenic lipoid-soluble substances)—this is increased in Cushing's syndrome; intravenous pyelography, which may suggest unilateral adrenal enlargement; and perinephric air insufflation with radiography in order to outline the adrenal glands (though this investigation, originating in the United States, has now apparently fallen into disuse there). As an extreme measure,

exploratory laparotomy followed by unilateral adrenalectomy—or removal of the adrenal tumour in the unlikely event of one being found—might be regarded as justifiable.

Gold in Rheumatoid Arthritis Complicated by Diabetes

Q.—*Is gold treatment absolutely contraindicated in a well-controlled diabetic with rheumatoid arthritis? If so, why?*

A.—Treatment with gold does entail some risk to a diabetic, as it may cause a dermatitis. If this occurs glycosuria and hyperglycaemia would probably occur, necessitating an increase in the insulin dosage. If gold is given a careful watch must be kept, both by the doctor and the patient, for a rash, as this may be very transient at its first appearance. If either an increase in the insulin requirements or a rash appears the gold treatment must be stopped at once. If very quickly the condition of the skin improves and the insulin requirement falls it may be possible to restart the gold injections with smaller doses and at longer intervals, but the risk is now considerably greater.

Quaternary Ammonium Compounds in Disseminated Sclerosis

Q.—*Are quaternary ammonium compounds useful in the treatment of disseminated sclerosis?*

A.—Many substances with a vasodilator action have been tried in the treatment of disseminated sclerosis, such as anti-adrenaline substances (often called adrenolytic or sympatholytic) and substances depressing transmission of constrictor impulses through ganglia (often called ganglion-blocking agents). One of the latter is tetraethylammonium chloride. In 1948 Bell, Williams, and Karnosh (*Cleveland Clin. Quart.*, 1948, **15**, 90) carried out a therapeutic trial of tetraethylammonium chloride in 22 patients, based on the hypothesis that the lesions of multiple sclerosis were due to a "vascular disorder such as haemostasis or change in vasomotor tone leading to thrombosis." Fourteen of the patients had a history of exacerbations and remissions, displaying acute signs such as transient scotomas, diplopia, numbness, paraesthesias, weakness of extremities, urinary incontinence, dysarthria, astereognosis, and ataxia. The drug was given in 500- to 1,200-mg. doses intramuscularly three to six times a week. Acute symptoms are said to have responded. Intermittent scotomas were promptly relieved in one patient. Continued therapy in all instances appeared to have protected patients from relapses or further progress of symptoms. The longest period of freedom from symptoms was five months. In all 14 patients with acute symptoms definite improvement in the most recently acquired symptoms occurred within four days after the start of therapy. It was pointed out that despite spontaneous and unpredictable remissive factors it is unlikely that 14 spontaneous remissions would have occurred so shortly after the institution of treatment. Eight patients with chronic manifestations that had been static for six months prior to therapy were not benefited. It was concluded that tetraethylammonium chloride was probably not of value for the prevention of further relapses once it was discontinued, and that the small number of patients and the brief period of observation did not offer convincing proof that the drug entirely controlled transitory symptoms of multiple sclerosis. Individual protocols were not given. An extension of this study to more than 300 patients with multiple sclerosis has not revealed lasting benefit. The drug is said not to prevent further attacks or to affect the prognosis materially, though over half the patients claim improvement during the first five days of treatment.

Recently Fisher (*N.Y. St. J. Med.*, 1949, **49**, 1033) studied more than 50 patients who have had multiple sclerosis for 3 to 15 years. Treatment has not been continued long enough to evaluate results. Preliminary investigations are said to be sufficiently encouraging to warrant further trial.

Thus, despite the wide application of vasodilator therapy, there is lack of conclusive data regarding its efficacy. Although the use of such substances has theoretical justification, there is no evidence from which we can predict results with certainty.

Inheritance of Cooley's Anaemia

Q.—*An only child of Greek parents has had Cooley's anaemia since birth. What are the chances that a second child will suffer from that disease?*

A.—Cooley's anaemia, or thalassaemia, is due to a recessive gene which is relatively common in some Mediterranean races, including the Greeks. The chance that a second child of these parents will be similarly affected is one in four.

Lumbago

Q.—*Where can I find information on the pathology of lumbago?*

A.—On p. 181 of the book "*Any Questions?*" The book can be obtained for 7s. 6d. (postage 6d.) from the Publishing Manager, B.M.A. House, Tavistock Square, W.C.1.

NOTES AND COMMENTS

Proctalgia Fugax.—Dr. D. H. BETT (Jersey) writes: May one from almost fifty years of personal experience, add two points to the answer to the question on proctalgia fugax ("Any Questions?" March 22, p. 669)? The simplest and generally quite effective treatment is to evoke reflex relaxation by eating a couple of biscuits. Secondly, as one gets older attacks become milder and less frequent.

Dr. TREVOR HUGHES (Ruthin) writes: Your expert's explanation of the cause of the condition is probably correct, and of all the muscles indicted I think the internal sphincter is probably the most likely offender. The remedies suggested, however, seem to be impracticable in most households. Some years ago you advised a drink of cold water to relieve the spasm of proctalgia, and this has been very effective, to my knowledge, in some cases.

Mr. M. D. SHEPPARD, F.R.C.S. (Chelmsford), writes: Having suffered personally for some years all the unpleasant manifestations of proctalgia fugax, I was particularly interested to read your expert's reply. He suggests that the condition is partly of functional origin, but as the pain often wakes one from a good sleep I am just wondering how far this can be true. In my case the trouble is frequently brought on by excessive physical strain and occasionally a very hot bath. It is my impression that the condition is caused by thrombosis of a small external haemorrhoidal vein just at the ano-rectal junction, as a small tender swelling usually becomes apparent some while after the pain has passed. This evidence has been further confirmed by the fact that I have been able to cut short the spasm by firm pressure with the finger on the apparent site of the trouble.

Dr. MICHAEL ROPER (York) writes: I suffered from the symptoms described for some four to five years. The more severe attacks even reached the lower abdomen. Moreover, the anal and coccygeal regions were embarrassingly itchy. The cause became obvious when I developed a pilonidal sinus last year. Since its excision I have been entirely free from symptoms.

OUR EXPERT replies: I have little to add to these comments. I am convinced that most cases of proctalgia fugax occur with no abnormality whatsoever in the rectum or anal canal. Overwork and worry are common causes.

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